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(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF LUNG CANCER

(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly lung cancer, are disclosed. Illustrative compositions comprise one or more lung tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly lung cancer.



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## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF LUNG CANCER

### TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of  
5 cancer, such as lung cancer. The invention is more specifically related to polypeptides,  
comprising at least a portion of a lung tumor protein, and to polynucleotides encoding  
such polypeptides. Such polypeptides and polynucleotides are useful in pharmaceutical  
compositions, *e.g.*, vaccines, and other compositions for the diagnosis and treatment of  
lung cancer.

### 10 BACKGROUND OF THE INVENTION

Lung cancer is the primary cause of cancer death among both men and  
women in the U.S., with an estimated 172,000 new cases being reported in 1994. The  
five-year survival rate among all lung cancer patients, regardless of the stage of disease  
at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among  
15 cases detected while the disease is still localized. However, only 16% of lung cancers  
are discovered before the disease has spread.

Early detection is difficult since clinical symptoms are often not seen  
until the disease has reached an advanced stage. Currently, diagnosis is aided by the  
use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic  
20 examination of the bronchial passages. Treatment regimens are determined by the type  
and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In  
spite of considerable research into therapies for the disease, lung cancer remains  
difficult to treat.

Accordingly, there remains a need in the art for improved vaccines,  
25 treatment methods and diagnostic techniques for lung cancer.

### SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide  
compositions comprising a sequence selected from the group consisting of:

- (a) sequences provided in SEQ ID NO: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583;
- (b) complements of the sequences provided in SEQ ID NO: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583;
- 5 (c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583;
- (d) sequences that hybridize to a sequence provided in SEQ ID NO: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583, under moderately  
10 stringent conditions;
- (e) sequences having at least 75% identity to a sequence of SEQ ID NO: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583;
- (f) sequences having at least 90% identity to a sequence of SEQ ID NO: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583; and
- 15 (g) degenerate variants of a sequence provided in SEQ ID NO: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of lung tumors samples tested, at a level that  
20 is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

25 In specific embodiments, the present invention provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 391, 393, 395, 397, 421, 425-427, 434-439 and 584-587.

In certain preferred embodiments, the polypeptides and/or  
30 polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of

eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NOs: 391, 393, 395, 397, 421, 425-427, 434-439 and 584-587 or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NOs: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, the pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.



Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins  
5 that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins, typically in the form of pharmaceutical compositions, *e.g.*, vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise  
10 one or more polypeptide segments for facilitating the expression, purification and/or immunogenicity of the polypeptide(s).

Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The  
15 patient may be afflicted with lung cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a  
20 patient a pharmaceutical composition as recited above. The patient may be afflicted with lung cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological  
25 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological  
30 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer, preferably a lung cancer, in a patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time

- with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount  
5 detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

- The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that  
10 hybridizes to a polynucleotide that encodes a polypeptide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount  
15 of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as  
20 recited above, or a complement of such a polynucleotide.

- In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a polypeptide of the present invention; (b) detecting in the sample an amount of  
25 a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

- 5                These and other aspects of the present invention will become apparent upon reference to the following detailed description. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

#### SEQUENCE IDENTIFIERS

- 10                SEQ ID NO: 1 is the determined cDNA sequence for L363C1.cons  
                  SEQ ID NO: 2 is the determined cDNA sequence for L263C2.cons  
                  SEQ ID NO: 3 is the determined cDNA sequence for L263C2c  
                  SEQ ID NO: 4 is the determined cDNA sequence for L263C1.cons  
                  SEQ ID NO: 5 is the determined cDNA sequence for L263C1b  
15                SEQ ID NO: 6 is the determined cDNA sequence for L164C2.cons  
                  SEQ ID NO: 7 is the determined cDNA sequence for L164C1.cons  
                  SEQ ID NO: 8 is the determined cDNA sequence for L366C1a  
                  SEQ ID NO: 9 is the determined cDNA sequence for L260C1.cons  
                  SEQ ID NO: 10 is the determined cDNA sequence for L163C1c  
20                SEQ ID NO: 11 is the determined cDNA sequence for L163C1b  
                  SEQ ID NO: 12 is the determined cDNA sequence for L255C1.cons  
                  SEQ ID NO: 13 is the determined cDNA sequence for L255C1b  
                  SEQ ID NO: 14 is the determined cDNA sequence for L355C1.cons  
                  SEQ ID NO: 15 is the determined cDNA sequence for L366C1.cons  
25                SEQ ID NO: 16 is the determined cDNA sequence for L163C1a  
                  SEQ ID NO: 17 is the determined cDNA sequence for LT86-1  
                  SEQ ID NO: 18 is the determined cDNA sequence for LT86-2  
                  SEQ ID NO: 19 is the determined cDNA sequence for LT86-3  
                  SEQ ID NO: 20 is the determined cDNA sequence for LT86-4

- SEQ ID NO: 21 is the determined cDNA sequence for LT86-5
- SEQ ID NO: 22 is the determined cDNA sequence for LT86-6
- SEQ ID NO: 23 is the determined cDNA sequence for LT86-7
- SEQ ID NO: 24 is the determined cDNA sequence for LT86-8
- 5 SEQ ID NO: 25 is the determined cDNA sequence for LT86-9
- SEQ ID NO: 26 is the determined cDNA sequence for LT86-10
- SEQ ID NO: 27 is the determined cDNA sequence for LT86-11
- SEQ ID NO: 28 is the determined cDNA sequence for LT86-12
- SEQ ID NO: 29 is the determined cDNA sequence for LT86-13
- 10 SEQ ID NO: 30 is the determined cDNA sequence for LT86-14
- SEQ ID NO: 31 is the determined cDNA sequence for LT86-15
- SEQ ID NO: 32 is the predicted amino acid sequence for LT86-1
- SEQ ID NO: 33 is the predicted amino acid sequence for LT86-2
- SEQ ID NO: 34 is the predicted amino acid sequence for LT86-3
- 15 SEQ ID NO: 35 is the predicted amino acid sequence for LT86-4
- SEQ ID NO: 36 is the predicted amino acid sequence for LT86-5
- SEQ ID NO: 37 is the predicted amino acid sequence for LT86-6
- SEQ ID NO: 38 is the predicted amino acid sequence for LT86-7
- SEQ ID NO: 39 is the predicted amino acid sequence for LT86-8
- 20 SEQ ID NO: 40 is the predicted amino acid sequence for LT86-9
- SEQ ID NO: 41 is the predicted amino acid sequence for LT86-10
- SEQ ID NO: 42 is the predicted amino acid sequence for LT86-11
- SEQ ID NO: 43 is the predicted amino acid sequence for LT86-12
- SEQ ID NO: 44 is the predicted amino acid sequence for LT86-13
- 25 SEQ ID NO: 45 is the predicted amino acid sequence for LT86-14
- SEQ ID NO: 46 is the predicted amino acid sequence for LT86-15
- SEQ ID NO: 47 is a (dT)<sub>12</sub>AG primer
- SEQ ID NO: 48 is a primer
- SEQ ID NO: 49 is the determined 5' cDNA sequence for L86S-3
- 30 SEQ ID NO: 50 is the determined 5' cDNA sequence for L86S-12

- SEQ ID NO: 51 is the determined 5' cDNA sequence for L86S-16  
SEQ ID NO: 52 is the determined 5' cDNA sequence for L86S-25  
SEQ ID NO: 53 is the determined 5' cDNA sequence for L86S-36  
SEQ ID NO: 54 is the determined 5' cDNA sequence for L86S-40  
5 SEQ ID NO: 55 is the determined 5' cDNA sequence for L86S-46  
SEQ ID NO: 56 is the predicted amino acid sequence for L86S-3  
SEQ ID NO: 57 is the predicted amino acid sequence for L86S-12  
SEQ ID NO: 58 is the predicted amino acid sequence for L86S-16  
SEQ ID NO: 59 is the predicted amino acid sequence for L86S-25  
10 SEQ ID NO: 60 is the predicted amino acid sequence for L86S-36  
SEQ ID NO: 61 is the predicted amino acid sequence for L86S-40  
SEQ ID NO: 62 is the predicted amino acid sequence for L86S-46  
SEQ ID NO: 63 is the determined 5' cDNA sequence for L86S-30  
SEQ ID NO: 64 is the determined 5' cDNA sequence for L86S-41  
15 SEQ ID NO: 65 is the predicted amino acid sequence from the 5' end of  
LT86-9  
SEQ ID NO: 66 is the determined extended cDNA sequence for LT86-4  
SEQ ID NO: 67 is the predicted extended amino acid sequence for  
LT86-4  
20 SEQ ID NO: 68 is the determined 5' cDNA sequence for LT86-20  
SEQ ID NO: 69 is the determined 3' cDNA sequence for LT86-21  
SEQ ID NO: 70 is the determined 5' cDNA sequence for LT86-22  
SEQ ID NO: 71 is the determined 5' cDNA sequence for LT86-26  
SEQ ID NO: 72 is the determined 5' cDNA sequence for LT86-27  
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SEQ ID NO: 74 is the predicted amino acid sequence for LT86-21  
SEQ ID NO: 75 is the predicted amino acid sequence for LT86-22  
SEQ ID NO: 76 is the predicted amino acid sequence for LT86-26  
SEQ ID NO: 77 is the predicted amino acid sequence for LT86-27  
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SEQ ID NO: 79 is the determined extended cDNA sequence for L86S-36

SEQ ID NO: 80 is the determined extended cDNA sequence for L86S-46

SEQ ID NO: 81 is the predicted extended amino acid sequence for  
L86S-12

5           SEQ ID NO: 82 is the predicted extended amino acid sequence for L86S-

36

          SEQ ID NO: 83 is the predicted extended amino acid sequence for  
L86S-46

SEQ ID NO: 84 is the determined 5' cDNA sequence for L86S-6

10          SEQ ID NO: 85 is the determined 5' cDNA sequence for L86S-11

SEQ ID NO: 86 is the determined 5' cDNA sequence for L86S-14

SEQ ID NO: 87 is the determined 5' cDNA sequence for L86S-29

SEQ ID NO: 88 is the determined 5' cDNA sequence for L86S-34

SEQ ID NO: 89 is the determined 5' cDNA sequence for L86S-39

15          SEQ ID NO: 90 is the determined 5' cDNA sequence for L86S-47

SEQ ID NO: 91 is the determined 5' cDNA sequence for L86S-49

SEQ ID NO: 92 is the determined 5' cDNA sequence for L86S-51

SEQ ID NO: 93 is the predicted amino acid sequence for L86S-6

SEQ ID NO: 94 is the predicted amino acid sequence for L86S-11

20          SEQ ID NO: 95 is the predicted amino acid sequence for L86S-14

SEQ ID NO: 96 is the predicted amino acid sequence for L86S-29

SEQ ID NO: 97 is the predicted amino acid sequence for L86S-34

SEQ ID NO: 98 is the predicted amino acid sequence for L86S-39

SEQ ID NO: 99 is the predicted amino acid sequence for L86S-47

25          SEQ ID NO: 100 is the predicted amino acid sequence for L86S-49

SEQ ID NO: 101 is the predicted amino acid sequence for L86S-51

SEQ ID NO: 102 is the determined DNA sequence for SLT-T1

SEQ ID NO: 103 is the determined 5' cDNA sequence for SLT-T2

SEQ ID NO: 104 is the determined 5' cDNA sequence for SLT-T3

30          SEQ ID NO: 105 is the determined 5' cDNA sequence for SLT-T5

- SEQ ID NO: 106 is the determined 5' cDNA sequence for SLT-T7  
SEQ ID NO: 107 is the determined 5' cDNA sequence for SLT-T9  
SEQ ID NO: 108 is the determined 5' cDNA sequence for SLT-T10  
SEQ ID NO: 109 is the determined 5' cDNA sequence for SLT-T11  
5 SEQ ID NO: 110 is the determined 5' cDNA sequence for SLT-T12  
SEQ ID NO: 111 is the predicted amino acid sequence for SLT-T1  
SEQ ID NO: 112 is the predicted amino acid sequence for SLT-T2  
SEQ ID NO: 113 is the predicted amino acid sequence for SLT-T3  
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10 SEQ ID NO: 115 is the predicted amino acid sequence for SLT-T12  
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SEQ ID NO: 127 is the determined cDNA sequence for PSLT-2  
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SEQ ID NO: 129 is the determined cDNA sequence for PSLT-13  
25 SEQ ID NO: 130 is the determined cDNA sequence for PSLT-27  
SEQ ID NO: 131 is the determined cDNA sequence for PSLT-28  
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SEQ ID NO: 133 is the determined cDNA sequence for PSLT-40  
SEQ ID NO: 134 is the determined cDNA sequence for PSLT-69  
30 SEQ ID NO: 135 is the determined cDNA sequence for PSLT-71



- SEQ ID NO: 136 is the determined cDNA sequence for PSLT-73  
SEQ ID NO: 137 is the determined cDNA sequence for PSLT-79  
SEQ ID NO: 138 is the determined cDNA sequence for PSLT-03  
SEQ ID NO: 139 is the determined cDNA sequence for PSLT-09  
5 SEQ ID NO: 140 is the determined cDNA sequence for PSLT-011  
SEQ ID NO: 141 is the determined cDNA sequence for PSLT-041  
SEQ ID NO: 142 is the determined cDNA sequence for PSLT-62  
SEQ ID NO: 143 is the determined cDNA sequence for PSLT-6  
SEQ ID NO: 144 is the determined cDNA sequence for PSLT-37  
10 SEQ ID NO: 145 is the determined cDNA sequence for PSLT-74  
SEQ ID NO: 146 is the determined cDNA sequence for PSLT-010  
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SEQ ID NO: 148 is the determined cDNA sequence for PSLT-037  
SEQ ID NO: 149 is the determined 5' cDNA sequence for SAL-3  
15 SEQ ID NO: 150 is the determined 5' cDNA sequence for SAL-24  
SEQ ID NO: 151 is the determined 5' cDNA sequence for SAL-25  
SEQ ID NO: 152 is the determined 5' cDNA sequence for SAL-33  
SEQ ID NO: 153 is the determined 5' cDNA sequence for SAL-50  
SEQ ID NO: 154 is the determined 5' cDNA sequence for SAL-57  
20 SEQ ID NO: 155 is the determined 5' cDNA sequence for SAL-66  
SEQ ID NO: 156 is the determined 5' cDNA sequence for SAL-82  
SEQ ID NO: 157 is the determined 5' cDNA sequence for SAL-99  
SEQ ID NO: 158 is the determined 5' cDNA sequence for SAL-104  
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SEQ ID NO: 161 is the determined 5' cDNA sequence for SAL-8  
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SEQ ID NO: 164 is the determined 5' cDNA sequence for SAL-16  
30 SEQ ID NO: 165 is the determined 5' cDNA sequence for SAL-23

- SEQ ID NO: 166 is the determined 5' cDNA sequence for SAL-26
- SEQ ID NO: 167 is the determined 5' cDNA sequence for SAL-29
- SEQ ID NO: 168 is the determined 5' cDNA sequence for SAL-32
- SEQ ID NO: 169 is the determined 5' cDNA sequence for SAL-39
- 5 SEQ ID NO: 170 is the determined 5' cDNA sequence for SAL-42
- SEQ ID NO: 171 is the determined 5' cDNA sequence for SAL-43
- SEQ ID NO: 172 is the determined 5' cDNA sequence for SAL-44
- SEQ ID NO: 173 is the determined 5' cDNA sequence for SAL-48
- SEQ ID NO: 174 is the determined 5' cDNA sequence for SAL-68
- 10 SEQ ID NO: 175 is the determined 5' cDNA sequence for SAL-72
- SEQ ID NO: 176 is the determined 5' cDNA sequence for SAL-77
- SEQ ID NO: 177 is the determined 5' cDNA sequence for SAL-86
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- SEQ ID NO: 181 is the determined 5' cDNA sequence for SAL-105
- SEQ ID NO: 182 is the predicted amino acid sequence for SAL-3
- SEQ ID NO: 183 is the predicted amino acid sequence for SAL-24
- SEQ ID NO: 184 is a first predicted amino acid sequence for SAL-25
- 20 SEQ ID NO: 185 is a second predicted amino acid sequence for SAL-25
- SEQ ID NO: 186 is the predicted amino acid sequence for SAL-33
- SEQ ID NO: 187 is a first predicted amino acid sequence for SAL-50
- SEQ ID NO: 188 is the predicted amino acid sequence for SAL-57
- SEQ ID NO: 189 is a first predicted amino acid sequence for SAL-66
- 25 SEQ ID NO: 190 is a second predicted amino acid sequence for SAL-66
- SEQ ID NO: 191 is the predicted amino acid sequence for SAL-82
- SEQ ID NO: 192 is the predicted amino acid sequence for SAL-99
- SEQ ID NO: 193 is the predicted amino acid sequence for SAL-104
- SEQ ID NO: 194 is the predicted amino acid sequence for SAL-5
- 30 SEQ ID NO: 195 is the predicted amino acid sequence for SAL-8

- SEQ ID NO: 196 is the predicted amino acid sequence for SAL-12
- SEQ ID NO: 197 is the predicted amino acid sequence for SAL-14
- SEQ ID NO: 198 is the predicted amino acid sequence for SAL-16
- SEQ ID NO: 199 is the predicted amino acid sequence for SAL-23
- 5 SEQ ID NO: 200 is the predicted amino acid sequence for SAL-26
- SEQ ID NO: 201 is the predicted amino acid sequence for SAL-29
- SEQ ID NO: 202 is the predicted amino acid sequence for SAL-32
- SEQ ID NO: 203 is the predicted amino acid sequence for SAL-39
- SEQ ID NO: 204 is the predicted amino acid sequence for SAL-42
- 10 SEQ ID NO: 205 is the predicted amino acid sequence for SAL-43
- SEQ ID NO: 206 is the predicted amino acid sequence for SAL-44
- SEQ ID NO: 207 is the predicted amino acid sequence for SAL-48
- SEQ ID NO: 208 is the predicted amino acid sequence for SAL-68
- SEQ ID NO: 209 is the predicted amino acid sequence for SAL-72
- 15 SEQ ID NO: 210 is the predicted amino acid sequence for SAL-77
- SEQ ID NO: 211 is the predicted amino acid sequence for SAL-86
- SEQ ID NO: 212 is the predicted amino acid sequence for SAL-88
- SEQ ID NO: 213 is the predicted amino acid sequence for SAL-93
- SEQ ID NO: 214 is the predicted amino acid sequence for SAL-100
- 20 SEQ ID NO: 215 is the predicted amino acid sequence for SAL-105
- SEQ ID NO: 216 is a second predicted amino acid sequence for SAL-50
- SEQ ID NO: 217 is the determined cDNA sequence for SSLT-4
- SEQ ID NO: 218 is the determined cDNA sequence for SSLT-9
- SEQ ID NO: 219 is the determined cDNA sequence for SSLT-10
- 25 SEQ ID NO: 220 is the determined cDNA sequence for SSLT-12
- SEQ ID NO: 221 is the determined cDNA sequence for SSLT-19
- SEQ ID NO: 222 is the determined cDNA sequence for SSLT-31
- SEQ ID NO: 223 is the determined cDNA sequence for SSLT-38
- SEQ ID NO: 224 is the determined cDNA sequence for LT4690-2
- 30 SEQ ID NO: 225 is the determined cDNA sequence for LT4690-3

- SEQ ID NO: 226 is the determined cDNA sequence for LT4690-22  
SEQ ID NO: 227 is the determined cDNA sequence for LT4690-24  
SEQ ID NO: 228 is the determined cDNA sequence for LT4690-37  
SEQ ID NO: 229 is the determined cDNA sequence for LT4690-39  
5 SEQ ID NO: 230 is the determined cDNA sequence for LT4690-40  
SEQ ID NO: 231 is the determined cDNA sequence for LT4690-41  
SEQ ID NO: 232 is the determined cDNA sequence for LT4690-49  
SEQ ID NO: 233 is the determined 3' cDNA sequence for LT4690-55  
SEQ ID NO: 234 is the determined 5' cDNA sequence for LT4690-55  
10 SEQ ID NO: 235 is the determined cDNA sequence for LT4690-59  
SEQ ID NO: 236 is the determined cDNA sequence for LT4690-63  
SEQ ID NO: 237 is the determined cDNA sequence for LT4690-71  
SEQ ID NO: 238 is the determined cDNA sequence for 2LT-3  
SEQ ID NO: 239 is the determined cDNA sequence for 2LT-6  
15 SEQ ID NO: 240 is the determined cDNA sequence for 2LT-22  
SEQ ID NO: 241 is the determined cDNA sequence for 2LT-25  
SEQ ID NO: 242 is the determined cDNA sequence for 2LT-26  
SEQ ID NO: 243 is the determined cDNA sequence for 2LT-31  
SEQ ID NO: 244 is the determined cDNA sequence for 2LT-36  
20 SEQ ID NO: 245 is the determined cDNA sequence for 2LT-42  
SEQ ID NO: 246 is the determined cDNA sequence for 2LT-44  
SEQ ID NO: 247 is the determined cDNA sequence for 2LT-54  
SEQ ID NO: 248 is the determined cDNA sequence for 2LT-55  
SEQ ID NO: 249 is the determined cDNA sequence for 2LT-57  
25 SEQ ID NO: 250 is the determined cDNA sequence for 2LT-58  
SEQ ID NO: 251 is the determined cDNA sequence for 2LT-59  
SEQ ID NO: 252 is the determined cDNA sequence for 2LT-62  
SEQ ID NO: 253 is the determined cDNA sequence for 2LT-63  
SEQ ID NO: 254 is the determined cDNA sequence for 2LT-65  
30 SEQ ID NO: 255 is the determined cDNA sequence for 2LT-66

- SEQ ID NO: 256 is the determined cDNA sequence for 2LT-70
- SEQ ID NO: 257 is the determined cDNA sequence for 2LT-73
- SEQ ID NO: 258 is the determined cDNA sequence for 2LT-74
- SEQ ID NO: 259 is the determined cDNA sequence for 2LT-76
- 5 SEQ ID NO: 260 is the determined cDNA sequence for 2LT-77
- SEQ ID NO: 261 is the determined cDNA sequence for 2LT-78
- SEQ ID NO: 262 is the determined cDNA sequence for 2LT-80
- SEQ ID NO: 263 is the determined cDNA sequence for 2LT-85
- SEQ ID NO: 264 is the determined cDNA sequence for 2LT-87
- 10 SEQ ID NO: 265 is the determined cDNA sequence for 2LT-89
- SEQ ID NO: 266 is the determined cDNA sequence for 2LT-94
- SEQ ID NO: 267 is the determined cDNA sequence for 2LT-95
- SEQ ID NO: 268 is the determined cDNA sequence for 2LT-98
- SEQ ID NO: 269 is the determined cDNA sequence for 2LT-100
- 15 SEQ ID NO: 270 is the determined cDNA sequence for 2LT-103
- SEQ ID NO: 271 is the determined cDNA sequence for 2LT-105
- SEQ ID NO: 272 is the determined cDNA sequence for 2LT-107
- SEQ ID NO: 273 is the determined cDNA sequence for 2LT-108
- SEQ ID NO: 274 is the determined cDNA sequence for 2LT-109
- 20 SEQ ID NO: 275 is the determined cDNA sequence for 2LT-118
- SEQ ID NO: 276 is the determined cDNA sequence for 2LT-120
- SEQ ID NO: 277 is the determined cDNA sequence for 2LT-121
- SEQ ID NO: 278 is the determined cDNA sequence for 2LT-122
- SEQ ID NO: 279 is the determined cDNA sequence for 2LT-124
- 25 SEQ ID NO: 280 is the determined cDNA sequence for 2LT-126
- SEQ ID NO: 281 is the determined cDNA sequence for 2LT-127
- SEQ ID NO: 282 is the determined cDNA sequence for 2LT-128
- SEQ ID NO: 283 is the determined cDNA sequence for 2LT-129
- SEQ ID NO: 284 is the determined cDNA sequence for 2LT-133
- 30 SEQ ID NO: 285 is the determined cDNA sequence for 2LT-137

SEQ ID NO: 286 is the determined cDNA sequence for LT4690-71  
SEQ ID NO: 287 is the determined cDNA sequence for LT4690-82  
SEQ ID NO: 288 is the determined full-length cDNA sequence for

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- 5           SEQ ID NO: 289 is the determined cDNA sequence for SSLT-78  
          SEQ ID NO: 290 is the determined cDNA sequence for SCC1-8.  
          SEQ ID NO: 291 is the determined cDNA sequence for SCC1-12.  
          SEQ ID NO: 292 is the determined cDNA sequence for SCC1-336  
          SEQ ID NO: 293 is the determined cDNA sequence for SCC1-344
- 10          SEQ ID NO: 294 is the determined cDNA sequence for SCC1-345  
          SEQ ID NO: 295 is the determined cDNA sequence for SCC1-346  
          SEQ ID NO: 296 is the determined cDNA sequence for SCC1-348  
          SEQ ID NO: 297 is the determined cDNA sequence for SCC1-350  
          SEQ ID NO: 298 is the determined cDNA sequence for SCC1-352
- 15          SEQ ID NO: 299 is the determined cDNA sequence for SCC1-354  
          SEQ ID NO: 300 is the determined cDNA sequence for SCC1-355  
          SEQ ID NO: 301 is the determined cDNA sequence for SCC1-356  
          SEQ ID NO: 302 is the determined cDNA sequence for SCC1-357  
          SEQ ID NO: 303 is the determined cDNA sequence for SCC1-501
- 20          SEQ ID NO: 304 is the determined cDNA sequence for SCC1-503  
          SEQ ID NO: 305 is the determined cDNA sequence for SCC1-513  
          SEQ ID NO: 306 is the determined cDNA sequence for SCC1-516  
          SEQ ID NO: 307 is the determined cDNA sequence for SCC1-518  
          SEQ ID NO: 308 is the determined cDNA sequence for SCC1-519
- 25          SEQ ID NO: 309 is the determined cDNA sequence for SCC1-522  
          SEQ ID NO: 310 is the determined cDNA sequence for SCC1-523  
          SEQ ID NO: 311 is the determined cDNA sequence for SCC1-525  
          SEQ ID NO: 312 is the determined cDNA sequence for SCC1-527  
          SEQ ID NO: 313 is the determined cDNA sequence for SCC1-529
- 30          SEQ ID NO: 314 is the determined cDNA sequence for SCC1-530

- SEQ ID NO: 315 is the determined cDNA sequence for SCC1-531  
SEQ ID NO: 316 is the determined cDNA sequence for SCC1-532  
SEQ ID NO: 317 is the determined cDNA sequence for SCC1-533  
SEQ ID NO: 318 is the determined cDNA sequence for SCC1-536  
5 SEQ ID NO: 319 is the determined cDNA sequence for SCC1-538  
SEQ ID NO: 320 is the determined cDNA sequence for SCC1-539  
SEQ ID NO: 321 is the determined cDNA sequence for SCC1-541  
SEQ ID NO: 322 is the determined cDNA sequence for SCC1-542  
SEQ ID NO: 323 is the determined cDNA sequence for SCC1-546  
10 SEQ ID NO: 324 is the determined cDNA sequence for SCC1-549  
SEQ ID NO: 325 is the determined cDNA sequence for SCC1-551  
SEQ ID NO: 326 is the determined cDNA sequence for SCC1-552  
SEQ ID NO: 327 is the determined cDNA sequence for SCC1-554  
SEQ ID NO: 328 is the determined cDNA sequence for SCC1-558  
15 SEQ ID NO: 329 is the determined cDNA sequence for SCC1-559  
SEQ ID NO: 330 is the determined cDNA sequence for SCC1-561  
SEQ ID NO: 331 is the determined cDNA sequence for SCC1-562  
SEQ ID NO: 332 is the determined cDNA sequence for SCC1-564  
SEQ ID NO: 333 is the determined cDNA sequence for SCC1-565  
20 SEQ ID NO: 334 is the determined cDNA sequence for SCC1-566  
SEQ ID NO: 335 is the determined cDNA sequence for SCC1-567  
SEQ ID NO: 336 is the determined cDNA sequence for SCC1-568  
SEQ ID NO: 337 is the determined cDNA sequence for SCC1-570  
SEQ ID NO: 338 is the determined cDNA sequence for SCC1-572  
25 SEQ ID NO: 339 is the determined cDNA sequence for SCC1-575  
SEQ ID NO: 340 is the determined cDNA sequence for SCC1-576  
SEQ ID NO: 341 is the determined cDNA sequence for SCC1-577  
SEQ ID NO: 342 is the determined cDNA sequence for SCC1-578  
SEQ ID NO: 343 is the determined cDNA sequence for SCC1-582  
30 SEQ ID NO: 344 is the determined cDNA sequence for SCC1-583

- SEQ ID NO: 345 is the determined cDNA sequence for SCC1-586
- SEQ ID NO: 346 is the determined cDNA sequence for SCC1-588
- SEQ ID NO: 347 is the determined cDNA sequence for SCC1-590
- SEQ ID NO: 348 is the determined cDNA sequence for SCC1-591
- 5 SEQ ID NO: 349 is the determined cDNA sequence for SCC1-592
- SEQ ID NO: 350 is the determined cDNA sequence for SCC1-593
- SEQ ID NO: 351 is the determined cDNA sequence for SCC1-594
- SEQ ID NO: 352 is the determined cDNA sequence for SCC1-595
- SEQ ID NO: 353 is the determined cDNA sequence for SCC1-596
- 10 SEQ ID NO: 354 is the determined cDNA sequence for SCC1-598
- SEQ ID NO: 355 is the determined cDNA sequence for SCC1-599
- SEQ ID NO: 356 is the determined cDNA sequence for SCC1-602
- SEQ ID NO: 357 is the determined cDNA sequence for SCC1-604
- SEQ ID NO: 358 is the determined cDNA sequence for SCC1-605
- 15 SEQ ID NO: 359 is the determined cDNA sequence for SCC1-606
- SEQ ID NO: 360 is the determined cDNA sequence for SCC1-607
- SEQ ID NO: 361 is the determined cDNA sequence for SCC1-608
- SEQ ID NO: 362 is the determined cDNA sequence for SCC1-610
- SEQ ID NO: 363 is the determined cDNA sequence for clone DMS79T1
- 20 SEQ ID NO: 364 is the determined cDNA sequence for clone DMS79T2
- SEQ ID NO: 365 is the determined cDNA sequence for clone DMS79T3
- SEQ ID NO: 366 is the determined cDNA sequence for clone DMS79T5
- SEQ ID NO: 367 is the determined cDNA sequence for clone DMS79T6
- SEQ ID NO: 368 is the determined cDNA sequence for clone DMS79T7
- 25 SEQ ID NO: 369 is the determined cDNA sequence for clone DMS79T9
- SEQ ID NO: 370 is the determined cDNA sequence for clone
- DMS79T10
- SEQ ID NO: 371 is the determined cDNA sequence for clone
- DMS79T11
- 30 SEQ ID NO: 372 is the determined cDNA sequence for clone 128T1



- SEQ ID NO: 373 is the determined cDNA sequence for clone 128T2  
SEQ ID NO: 374 is the determined cDNA sequence for clone 128T3  
SEQ ID NO: 375 is the determined cDNA sequence for clone 128T4  
SEQ ID NO: 376 is the determined cDNA sequence for clone 128T5  
5 SEQ ID NO: 377 is the determined cDNA sequence for clone 128T7  
SEQ ID NO: 378 is the determined cDNA sequence for clone 128T9  
SEQ ID NO: 379 is the determined cDNA sequence for clone 128T10  
SEQ ID NO: 380 is the determined cDNA sequence for clone 128T11  
SEQ ID NO: 381 is the determined cDNA sequence for clone 128T12  
10 SEQ ID NO: 382 is the determined cDNA sequence for clone  
NCIH69T3  
SEQ ID NO: 383 is the determined cDNA sequence for clone  
NCIH69T5  
SEQ ID NO: 384 is the determined cDNA sequence for clone  
15 NCIH69T6  
SEQ ID NO: 385 is the determined cDNA sequence for clone  
NCIH69T7  
SEQ ID NO: 386 is the determined cDNA sequence for clone  
NCIH69T9  
20 SEQ ID NO: 387 is the determined cDNA sequence for clone  
NCIH69T10  
SEQ ID NO: 388 is the determined cDNA sequence for clone  
NCIH69T11  
SEQ ID NO: 389 is the determined cDNA sequence for clone  
25 NCIH69T12  
SEQ ID NO: 390 is the full-length cDNA sequence for 128T1  
SEQ ID NO: 391 is the amino acid sequence for 128T1  
SEQ ID NO: 392 is the full-length cDNA sequence for 2LT-128  
SEQ ID NO: 393 is the amino acid sequence for 2LT-128  
30 SEQ ID NO: 394 is an extended cDNA sequence for clone SCC1-542

- SEQ ID NO: 395 is the amino acid sequence corresponding to SEQ ID NO:394
- SEQ ID NO: 396 is an extended cDNA sequence for clone SCC1-593
- SEQ ID NO: 397 is the amino acid sequence corresponding to SEQ ID NO:396
- SEQ ID NO:398 is the determined cDNA sequence for 55508.1
- SEQ ID NO:399 is the determined cDNA sequence for 55509.1
- SEQ ID NO:400 is the determined cDNA sequence for 54243.1
- SEQ ID NO:401 is the determined cDNA sequence for 54251.1
- SEQ ID NO:402 is the determined cDNA sequence for 54252.1
- SEQ ID NO:403 is the determined cDNA sequence for 54253.1
- SEQ ID NO:404 is the determined cDNA sequence for 55518.1
- SEQ ID NO:405 is the determined cDNA sequence for 54258.1
- SEQ ID NO:406 is the determined cDNA sequence for 54575.1
- SEQ ID NO:407 is the determined cDNA sequence for 54577.1
- SEQ ID NO:408 is the determined cDNA sequence for 54584.1
- SEQ ID NO:409 is the determined cDNA sequence for 55521.1
- SEQ ID NO:410 is the determined cDNA sequence for 54589.1
- SEQ ID NO:411 is the determined cDNA sequence for 54592.1
- SEQ ID NO:412 is the determined cDNA sequence for 55134.1
- SEQ ID NO:413 is the determined cDNA sequence for 55137.1
- SEQ ID NO:414 is the determined cDNA sequence for 55140.1
- SEQ ID NO:415 is the determined cDNA sequence for 55531.1
- SEQ ID NO:416 is the determined cDNA sequence for 55532.1
- SEQ ID NO:417 is the determined cDNA sequence for 54621.1
- SEQ ID NO:418 is the determined cDNA sequence for 55548.1
- SEQ ID NO:419 is the determined cDNA sequence for 54623.1
- SEQ ID NO:420 is the determined cDNA sequence for L39
- SEQ ID NO:421 is the predicted amino acid sequence for L39
- SEQ ID NO:422 is the determined cDNA sequence for SCC2-29

- SEQ ID NO:423 is the determined cDNA sequence for SCC2-36
- SEQ ID NO:424 is the determined cDNA sequence for SCC2-60
- SEQ ID NO:425 is the predicted amino acid sequence for SCC2-29
- SEQ ID NO:426 is the predicted amino acid sequence for SCC2-36
- 5 SEQ ID NO:427 is the predicted amino acid sequence for SCC2-60
- SEQ ID NO:428 is an extended cDNA sequence for the clone 20129,  
also referred to as 2LT-3, set forth in SEQ ID NO: 238
- SEQ ID NO:429 is an extended cDNA sequence for the clone 20347,  
also referred to as 2LT-26, set forth in SEQ ID NO: 242
- 10 SEQ ID NO:430 is an extended cDNA sequence for the clone 21282,  
also referred to as 2LT-57, set forth in SEQ ID NO: 249
- SEQ ID NO:431 is an extended cDNA sequence for the clone 21283,  
also referred to as 2LT-58, set forth in SEQ ID NO: 250
- SEQ ID NO:432 is an extended cDNA sequence for the clone 21484,  
15 also referred to as 2LT-98, set forth in SEQ ID NO: 268
- SEQ ID NO:433 is an extended cDNA sequence for the clone 21871,  
also referred to as 2LT-124, set forth in SEQ ID NO: 279
- SEQ ID NO:434 is an amino acid sequence encoded by SEQ ID NO: 428
- SEQ ID NO:435 is an amino acid sequence encoded by SEQ ID NO: 429
- 20 SEQ ID NO:436 is an amino acid sequence encoded by SEQ ID NO: 430
- SEQ ID NO:437 is an amino acid sequence encoded by SEQ ID NO: 431
- SEQ ID NO:438 is an amino acid sequence encoded by SEQ ID NO: 432
- SEQ ID NO:439 is an amino acid sequence encoded by SEQ ID NO: 433
- SEQ ID NO:440 is the determined cDNA sequence for clone 19A4
- 25 SEQ ID NO: 441 is the determined full-length cDNA sequence for clone  
14F10.
- SEQ ID NO: 442 is the determined 5' cDNA sequence for clone 20E10.
- SEQ ID NO: 443 is a first determined cDNA sequence for clone 55153.
- SEQ ID NO: 444 is a second determined cDNA sequence for clone  
30 55153.

- SEQ ID NO: 445 is a first determined cDNA sequence for clone 55154.  
SEQ ID NO: 446 is a second determined cDNA sequence for clone 55154.
- 5 SEQ ID NO: 447 is the determined cDNA sequence for clone 55155.  
SEQ ID NO: 448 is a first determined cDNA sequence for clone 55156.  
SEQ ID NO: 449 is a second determined cDNA sequence for clone 55156.
- 10 SEQ ID NO: 450 is a first determined cDNA sequence for clone 55157.  
SEQ ID NO: 451 is a second determined cDNA sequence for clone 55157.
- SEQ ID NO: 452 is the determined cDNA sequence for clone 55158.  
SEQ ID NO: 453 is the determined cDNA sequence for clone 55159.  
SEQ ID NO: 454 is a first determined cDNA sequence for clone 55161.  
SEQ ID NO: 455 is a second determined cDNA sequence for clone 55161.
- 15 SEQ ID NO: 456 is a first determined cDNA sequence for clone 55162.  
SEQ ID NO: 457 is a second determined cDNA sequence for clone 55162.
- 20 SEQ ID NO: 458 is a first determined cDNA sequence for clone 55163.  
SEQ ID NO: 459 is a second determined cDNA sequence for clone 55163.
- SEQ ID NO: 460 is a first determined cDNA sequence for clone 55164.  
SEQ ID NO: 461 is a second determined cDNA sequence for clone 55164.
- 25 SEQ ID NO: 462 is a first determined cDNA sequence for clone 55165.  
SEQ ID NO: 463 is a second determined cDNA sequence for clone 55165.
- 30 SEQ ID NO: 464 is a first determined cDNA sequence for clone 55166.  
SEQ ID NO: 465 is a second determined cDNA sequence for clone 55166.

- SEQ ID NO: 466 is a first determined cDNA sequence for clone 55167.  
SEQ ID NO: 467 is a second determined cDNA sequence for clone 55167.
- 5 55168. SEQ ID NO: 468 is a first determined cDNA sequence for clone 55168.  
SEQ ID NO: 469 is a second determined cDNA sequence for clone 55168.
55169. SEQ ID NO: 470 is a first determined cDNA sequence for clone 55169.  
SEQ ID NO: 471 is a second determined cDNA sequence for clone 55169.
- 10 55170. SEQ ID NO: 472 is a first determined cDNA sequence for clone 55170.  
SEQ ID NO: 473 is a second determined cDNA sequence for clone 55170.
- 15 55171. SEQ ID NO: 474 is the determined cDNA sequence for clone 55171.  
SEQ ID NO: 475 is the determined cDNA sequence for clone 55172.  
SEQ ID NO: 476 is the determined cDNA sequence for clone 55173.  
SEQ ID NO: 477 is a first determined cDNA sequence for clone 55174.  
SEQ ID NO: 478 is a second determined cDNA sequence for clone 55174.
- 20 55175. SEQ ID NO: 479 is the determined cDNA sequence for clone 55175.  
SEQ ID NO: 480 is the determined cDNA sequence for clone 55176.  
SEQ ID NO: 481 is the determined cDNA sequence for contig 525.  
SEQ ID NO: 482 is the determined cDNA sequence for contig 526.  
SEQ ID NO: 483 is the determined cDNA sequence for contig 527.  
SEQ ID NO: 484 is the determined cDNA sequence for contig 528.
- 25 55176. SEQ ID NO: 485 is the determined cDNA sequence for contig 529.  
SEQ ID NO: 486 is the determined cDNA sequence for contig 530.  
SEQ ID NO: 487 is the determined cDNA sequence for contig 531.  
SEQ ID NO: 488 is the determined cDNA sequence for contig 532.  
SEQ ID NO: 489 is the determined cDNA sequence for contig 533.
- 30 55177. SEQ ID NO: 490 is the determined cDNA sequence for contig 534.

SEQ ID NO: 491 is the determined cDNA sequence for contig 535.  
SEQ ID NO: 492 is the determined cDNA sequence for contig 536.  
SEQ ID NO: 493 is the determined cDNA sequence for contig 537.  
SEQ ID NO: 494 is the determined cDNA sequence for contig 538.  
5 SEQ ID NO: 495 is the determined cDNA sequence for contig 539.  
SEQ ID NO: 496 is the determined cDNA sequence for contig 540.  
SEQ ID NO: 497 is the determined cDNA sequence for contig 541.  
SEQ ID NO: 498 is the determined cDNA sequence for contig 542.  
SEQ ID NO: 499 is the determined cDNA sequence for contig 543.  
10 SEQ ID NO: 500 is the determined cDNA sequence for contig 544.  
SEQ ID NO: 501 is the determined cDNA sequence for contig 545.  
SEQ ID NO: 502 is the determined cDNA sequence for contig 546.  
SEQ ID NO: 503 is the determined cDNA sequence for contig 547.  
SEQ ID NO: 504 is the determined cDNA sequence for contig 548.  
15 SEQ ID NO: 505 is the determined cDNA sequence for contig 549.  
SEQ ID NO: 506 is the determined cDNA sequence for contig 550.  
SEQ ID NO: 507 is the determined cDNA sequence for contig 551.  
SEQ ID NO: 508 is the determined cDNA sequence for contig 552.  
SEQ ID NO: 509 is the determined cDNA sequence for contig 553.  
20 SEQ ID NO: 510 is the determined cDNA sequence for contig 554.  
SEQ ID NO: 511 is the determined cDNA sequence for contig 555.  
SEQ ID NO: 512 is the determined cDNA sequence for clone 57207.  
SEQ ID NO: 513 is the determined cDNA sequence for clone 57209.  
SEQ ID NO: 514 is the determined cDNA sequence for clone 57210.  
25 SEQ ID NO: 515 is the determined cDNA sequence for clone 57211.  
SEQ ID NO: 516 is the determined cDNA sequence for clone 57212.  
SEQ ID NO: 517 is the determined cDNA sequence for clone 57213.  
SEQ ID NO: 518 is the determined cDNA sequence for clone 57215.  
SEQ ID NO: 519 is the determined cDNA sequence for clone 57219.  
30 SEQ ID NO: 520 is the determined cDNA sequence for clone 57221.

- SEQ ID NO: 521 is the determined cDNA sequence for clone 57222.  
SEQ ID NO: 522 is the determined cDNA sequence for clone 57223.  
SEQ ID NO: 523 is the determined cDNA sequence for clone 57225.  
SEQ ID NO: 524 is the determined cDNA sequence for clone 57227.  
5 SEQ ID NO: 525 is the determined cDNA sequence for clone 57228.  
SEQ ID NO: 526 is the determined cDNA sequence for clone 57229.  
SEQ ID NO: 527 is the determined cDNA sequence for clone 57230.  
SEQ ID NO: 528 is the determined cDNA sequence for clone 57231.  
SEQ ID NO: 529 is the determined cDNA sequence for clone 57232.  
10 SEQ ID NO: 530 is the determined cDNA sequence for clone 57233.  
SEQ ID NO: 531 is the determined cDNA sequence for clone 57234.  
SEQ ID NO: 532 is the determined cDNA sequence for clone 57235.  
SEQ ID NO: 533 is the determined cDNA sequence for clone 57236.  
SEQ ID NO: 534 is the determined cDNA sequence for clone 57237.  
15 SEQ ID NO: 535 is the determined cDNA sequence for clone 57238.  
SEQ ID NO: 536 is the determined cDNA sequence for clone 57239.  
SEQ ID NO: 537 is the determined cDNA sequence for clone 57240.  
SEQ ID NO: 538 is the determined cDNA sequence for clone 57242.  
SEQ ID NO: 539 is the determined cDNA sequence for clone 57243.  
20 SEQ ID NO: 540 is the determined cDNA sequence for clone 57245.  
SEQ ID NO: 541 is the determined cDNA sequence for clone 57248.  
SEQ ID NO: 542 is the determined cDNA sequence for clone 57249.  
SEQ ID NO: 543 is the determined cDNA sequence for clone 57250.  
SEQ ID NO: 544 is the determined cDNA sequence for clone 57251.  
25 SEQ ID NO: 545 is the determined cDNA sequence for clone 57253.  
SEQ ID NO: 546 is the determined cDNA sequence for clone 57254.  
SEQ ID NO: 547 is the determined cDNA sequence for clone 57255.  
SEQ ID NO: 548 is the determined cDNA sequence for clone 57257.  
SEQ ID NO: 549 is the determined cDNA sequence for clone 57258.  
30 SEQ ID NO: 550 is the determined cDNA sequence for clone 57259.

- SEQ ID NO: 551 is the determined cDNA sequence for clone 57261.  
SEQ ID NO: 552 is the determined cDNA sequence for clone 57262.  
SEQ ID NO: 553 is the determined cDNA sequence for clone 57263.  
SEQ ID NO: 554 is the determined cDNA sequence for clone 57264.  
5 SEQ ID NO: 555 is the determined cDNA sequence for clone 57265.  
SEQ ID NO: 556 is the determined cDNA sequence for clone 57266.  
SEQ ID NO: 557 is the determined cDNA sequence for clone 57267.  
SEQ ID NO: 558 is the determined cDNA sequence for clone 57268.  
SEQ ID NO: 559 is the determined cDNA sequence for clone 57269.  
10 SEQ ID NO: 560 is the determined cDNA sequence for clone 57270.  
SEQ ID NO: 561 is the determined cDNA sequence for clone 57271.  
SEQ ID NO: 562 is the determined cDNA sequence for clone 57272.  
SEQ ID NO: 563 is the determined cDNA sequence for clone 57274.  
SEQ ID NO: 564 is the determined cDNA sequence for clone 57275.  
15 SEQ ID NO: 565 is the determined cDNA sequence for clone 57277.  
SEQ ID NO: 566 is the determined cDNA sequence for clone 57280.  
SEQ ID NO: 567 is the determined cDNA sequence for clone 57281.  
SEQ ID NO: 568 is the determined cDNA sequence for clone 57282.  
SEQ ID NO: 569 is the determined cDNA sequence for clone 57283.  
20 SEQ ID NO: 570 is the determined cDNA sequence for clone 57285.  
SEQ ID NO: 571 is the determined cDNA sequence for clone 57287.  
SEQ ID NO: 572 is the determined cDNA sequence for clone 57288.  
SEQ ID NO: 573 is the determined cDNA sequence for clone 57289.  
SEQ ID NO: 574 is the determined cDNA sequence for clone 57290.  
25 SEQ ID NO: 575 is the determined cDNA sequence for clone 57292.  
SEQ ID NO: 576 is the determined cDNA sequence for clone 57295.  
SEQ ID NO: 577 is the determined cDNA sequence for clone 57296.  
SEQ ID NO: 578 is the determined cDNA sequence for clone 57297.  
SEQ ID NO: 579 is the determined cDNA sequence for clone 57299.  
30 SEQ ID NO: 580 is the determined cDNA sequence for clone 57301.



SEQ ID NO: 581 is the determined cDNA sequence for clone 57302.

SEQ ID NO: 582 is the determined cDNA sequence for the beta chain of a lung tumor specific T cell receptor.

SEQ ID NO: 583 is the determined cDNA sequence for the alpha chain of a lung tumor specific T cell receptor.

SEQ ID NO: 584 is the amino acid sequence encoded by SEQ ID NO: 583.

SEQ ID NO: 585 is the amino acid sequence encoded by SEQ ID NO: 582.

SEQ ID NO: 586 is the amino acid sequence encoded by the 5' terminus of 14F10.

SEQ ID NO: 587 is the amino acid sequence of a T cell epitope contained within SEQ ID NO: 586.

#### DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly lung cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (*e.g.*, T cells).

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); Maniatis et al. *Molecular Cloning: A Laboratory Manual* (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); *Oligonucleotide Synthesis* (N. Gait, ed., 1984); *Nucleic Acid Hybridization* (B. Hames & S. Higgins, eds., 1985); *Transcription and Translation* (B.

Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

All publications, patents and patent applications cited herein, whether supra or infra, are hereby incorporated by reference in their entirety.

- 5 As used in this specification and the appended claims, the singular forms “a,” “an” and “the” include plural references unless the content clearly dictates otherwise.

#### Polypeptide Compositions

- As used herein, the term “polypeptide” is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of this invention are amino acid subsequences comprising epitopes, *i.e.*, antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.
- 10  
15  
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- Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide sequence set forth in any one of SEQ ID NOs: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583. Certain other illustrative polypeptides of the invention comprise amino acid sequences as set forth in any one of SEQ ID NOs: 391, 393, 395, 397, 421, 425-427, 434-439 and 584-587.
- 25

The polypeptides of the present invention are sometimes herein referred to as lung tumor proteins or lung tumor polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in lung tumor samples. Thus, a "lung tumor polypeptide" or "lung tumor protein," refers generally to a polypeptide sequence of the present invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed in a substantial proportion of lung tumor samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of lung tumor samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in normal tissues, as determined using a representative assay provided herein. A lung tumor polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

In certain preferred embodiments, the polypeptides of the invention are immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with lung cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide. Immunogenic portions may generally be identified using well known techniques, such

as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they  
5 specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that  
10 is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that  
15 have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain  
20 have been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells  
25 and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies  
30 that are immunologically reactive with one or more polypeptides described herein, or

one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

- 5           The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide compositions set forth herein, such as those set forth in SEQ ID NOs: 391, 393, 395, 397, 421, 425-427, 434-439 and 584-587, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID
- 10 NOs: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583.

- In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity
- 15 (determined as described below), along its length, to a polypeptide sequences set forth herein.

          In one preferred embodiment, the polypeptide fragments and variants provide by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set for the herein.

- 20           In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

- 25           A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of the above polypeptide sequences of the invention and evaluating their immunogenic

activity as described herein and/or using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A “conservative substitution” is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide with desirable characteristics, *e.g.*, with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein’s biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids				Codons					
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

- In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its

hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5);  
5 glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose  
10 hydropathic indices are within  $\pm 2$  is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by  
15 reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0  $\pm$  1); glutamate (+3.0  $\pm$  1); serine (+0.3); asparagine (+0.2); glutamine  
20 (+0.2); glycine (0); threonine (-0.4); proline (-0.5  $\pm$  1); alanine (-0.5); histidine (-0.5); cysteine (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5); tryptophan (-3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In  
25 such changes, the substitution of amino acids whose hydrophilicity values are within  $\pm 2$  is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their  
30 hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that



take various of the foregoing characteristics into consideration are well known to those of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

- In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

- Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the

polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be "identical" if the sequence of amino acids in the two sequences is the same when  
 5 aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a  
 10 reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several  
 15 alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology*  
 20 vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and  
 25 Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988)  
 30 *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these

algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises

at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

10 Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

20 A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors:

25 (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as

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linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second

5 polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding

10 the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein

15 capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12

20 fragment. Ra12 compositions and methods for their use in enhancing the expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid.

25 MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; *see also*, Skeiky et al., *Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding

30 sequence express at high levels and remain as a soluble polypeptides throughout the

purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally

5 comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a

10 sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about

15 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises

20 approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer).

25 The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein

30 known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is

derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible  
5 for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of  
10 LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting  
15 signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention, when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4<sup>+</sup> T-cells specific for the polypeptide.

20 Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are  
25 synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and  
30 may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of the invention are isolated. An "isolated" polypeptide is one that is removed from its original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, *e.g.*, are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure.

#### Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the



present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or  
5 may comprise a sequence that encodes a variant or derivative, preferably and immunogenic variant or derivative, of such a sequence.

Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 217-390, 392, 394, 396, 398-420 422-  
10 424, 428-433 and 440-583, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NOs: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583. In certain preferred embodiments, the polynucleotide sequences set forth herein encode  
15 immunogenic polypeptides, as described above.

In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 217-390, 392, 394, 396, 398-420 422-424, 428-433 and 440-583, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%,  
20 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this invention using the methods described herein, (*e.g.*, BLAST analysis using standard parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into  
25 account codon degeneracy, amino acid similarity, reading frame positioning and the like.

Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished  
30 relative to a polypeptide encoded by a polynucleotide sequence specifically set forth

herein). The term "variants" should also be understood to encompass homologous genes of xenogenic origin.

In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to or complementary to one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103, *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides

that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships.

- In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989)
- 5 *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.
  - 10 Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these
  - 15 algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

- One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0
- 20 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology
  - 25 Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero
  - 30 or below, due to the accumulation of one or more negative-scoring residue alignments;

or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of

immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25 nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known rules of complementary base pairing (see, for example, Watson, 1987). Typically,

vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

5 In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

10 In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 nucleotide long contiguous sequence that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence  
15 disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a  
20 sequence of interest will enable them to be of use in detecting the presence of complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of  
25 contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also  
30 in various bacterial cells. The total size of fragment, as well as the size of the



complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger  
5 contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in  
10 length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various  
20 factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be  
25 obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, *e.g.*, one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention, polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis is well established. For example, the synthesis of polygalacturonase and the muscarine

type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, 5 striatal GABA<sub>A</sub> receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a 10 variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a 15 complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In 20 each case, preferred compositions comprise a sequence region that is complementary, and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure,  $T_m$ , 25 binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary 30 to 5' regions of the mRNA. These secondary structure analyses and target site selection

considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997, 25(17):3389-402).

The use of an antisense delivery method employing a short peptide  
5 vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered  
10 into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme  
15 molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For  
20 example, a large number of ribozymes accelerate phosphoester transfer reactions with a high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement  
25 that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general,  
30 enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs

through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action (Woelf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead

- 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada *et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

- Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

- Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO 92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

- Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by

incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct  
5 inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO  
10 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for  
15 eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the  
20 prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as  
25 retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that  
30 traditionally have used RNA or DNA. Often PNA sequences perform better in

techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem*. 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*, *Bioorg Med Chem*. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed by the purification of PNAs by reverse-phase high-pressure liquid chromatography,



providing yields and purity of product similar to those observed during the synthesis of peptides.

- Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*, Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*, Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to therapeutics.

- Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of

transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

#### Polynucleotide Identification, Characterization and Expression

Polynucleotides compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by reference in its entirety. Briefly, in PCR™, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse

transcription and PCR<sup>TM</sup> amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR<sup>TM</sup> amplification technique, are readily known and available in the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat. Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara, 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (e.g., a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with <sup>32</sup>P) using well known techniques. A bacterial or

bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can then be assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl.*

*Acids. Res. 19:3055-60, 1991*). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction

sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to  
5 encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding  
10 sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical  
15 methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be confirmed by amino acid analysis or sequencing (e.g., the Edman  
25 degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

In order to express a desired polypeptide, the nucleotide sequences  
30 encoding the polypeptide, or functional equivalents, may be inserted into appropriate

expression vector, *i.e.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (*e.g.*, baculovirus); plant cell systems transformed with virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (*e.g.*, Ti or pBR322 plasmids); or animal cell systems.

The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains

multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example, when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of .beta.-galactosidase so that a hybrid protein is produced; pIN vectors (Van Hecke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991)



*Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion

thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic.

- 5 The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the  
10 desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular  
15 machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may  
20 contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which  
25 successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase  
30 (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or

aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies

specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; Serological Methods, a Laboratory Manual, APS Press, St Paul, Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are

- not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).
- 15 In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

#### Antibody Compositions, Fragments Thereof and Other Binding Agents

- 25 According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an

ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

- Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant ( $K_d$ ) of the interaction, wherein a smaller  $K_d$  represents a greater affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both the "on rate constant" ( $K_{on}$ ) and the "off rate constant" ( $K_{off}$ ) can be determined by calculation of the concentrations and the actual rates of association and dissociation.
- The ratio of  $K_{off}/K_{on}$  enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant  $K_d$ . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

- An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable regions" which are interposed between more conserved flanking stretches known as "framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen,

and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as lung cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a

superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically.

- 5 Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J.*

- 10 *Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a  
15 myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine,  
20 aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

- Monoclonal antibodies may be isolated from the supernatants of growing  
25 hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and



extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab)<sub>2</sub>" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V<sub>H</sub>::V<sub>L</sub> heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule.

15 Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V<sub>H</sub>::V<sub>L</sub> heterodimer which is expressed from a gene fusion including V<sub>H</sub>- and V<sub>L</sub>-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci.

20 USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an antigen-binding site. See, *e.g.*, U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.;

25 and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRs and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three

30 hypervariable regions of a heavy or light chain V region. Proceeding from the N-

terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (e.g., a CDR1, CDR2 or CDR3) is referred to herein as a  
5 "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

10 As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRs. Within FRs, certain amino residues and certain structural  
15 features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical"  
20 structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including  
25 chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) Nature 349:293-299; Lobuglio et al. (1989) Proc. Nat. Acad. Sci. USA 86:4220-4224; Shaw et al. (1987) J Immunol. 138:4534-4538; and Brown et al. (1987) Cancer Res. 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant  
30 domain (Riechmann et al. (1988) Nature 332:323-327; Verhoeven et al. (1988) Science

239:1534-1536; and Jones et al. (1986) Nature 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, e.g., a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) Ann. Rev. Biochem. 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (e.g., solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable

domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (e.g., electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a

substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

- 5 Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in  
10 chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

- It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker  
15 group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

- Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a  
20 linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of  
25 derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

- It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In  
30 another embodiment, more than one type of agent may be coupled to one antibody.

Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

- 5                   A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a
- 10                  liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be
- 15                  formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

### T Cell Compositions

- The present invention, in another aspect, provides T cells specific for a
- 20                  tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine,
- 25                  CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

                  T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide.

Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

- 5 T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of  
10 more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA  
15 synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as  
20 measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Tumor polypeptide-specific T  
25 cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

- For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number  
30 either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a

variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that  
5 proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

#### Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation  
10 of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other  
15 proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from  
20 host cells or other biological sources, or alternatively may be chemically synthesized as described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide,  
25 antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F.



Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

- 5 It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (e.g., salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases  
10 (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

- In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery  
15 systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable  
20 promoter and terminating signal). Alternatively, bacterial delivery systems may involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

- Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian  
25 host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered  
30 to a subject. A number of illustrative retroviral systems have been described (e.g., U.S.

Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

- 5           In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahriad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

- Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, e.g., U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines* 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-539; Muzyczka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129; 15           Kotin, R. M. (1994) *Human Gene Therapy* 5:793-801; Shelling and Smith (1994) *Gene Therapy* 1:165-169; and Zhou et al. (1994) *J. Exp. Med.* 179:1867-1875.

- Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of 25           example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. 30           Homologous recombination serves to insert the vaccinia promoter plus the gene

encoding the polypeptide of interest into the viral genome. The resulting TK<sub>sup</sub>(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or co-expression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected *in vitro* with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, *e.g.*, Elroy-Stein and Moss, Proc. Natl. Acad. Sci. USA (1990) 87:6743-6747; Fuerst et al. Proc. Natl. Acad. Sci. USA (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, *e.g.*, WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based

on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in the specific location and orientation via homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the polynucleotide may be stably maintained in the cell as a separate, episomal segment of DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK) and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device, propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes;

biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Within certain embodiments of the invention, the adjuvant composition is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL<sup>®</sup> adjuvants are available from Corixa Corporation (Seattle, WA; *see*, for example, US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example

combinations of at least two of the following group comprising QS21, QS7, Quil A,  $\beta$ -escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and  
5 polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix, particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated  
10 together with a polyoxyethylene ether or ester, in either a non-particulate solution or suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol<sup>®</sup> to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

15 In one preferred embodiment, the adjuvant system includes the combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL<sup>®</sup> adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in  
20 WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-MPL<sup>®</sup> adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

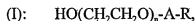
Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of  
25 CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series  
30 of adjuvants (e.g., SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart,

Belgium), Detox (Enhanzyn®) (Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and

5 polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



wherein,  $n$  is 1-50,  $A$  is a bond or  $-\text{C}(\text{O})-$ ,  $R$  is  $\text{C}_{1-50}$  alkyl or Phenyl  $\text{C}_{1-50}$  alkyl.

10 One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein  $n$  is between 1 and 50, preferably 4-24, most preferably 9; the  $R$  component is  $\text{C}_{1-50}$ , preferably  $\text{C}_4\text{-C}_{20}$  alkyl and most preferably  $\text{C}_{12}$  alkyl, and  $A$  is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably

15 from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck

20 index (12<sup>th</sup> edition: entry 7717). These adjuvant molecules are described in WO 99/52549.

The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application

25 GB 9820956.2.

According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified

30 to increase the capacity for presenting the antigen, to improve activation and/or



maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the

present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release. In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (e.g., a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (e.g., polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763; 5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (e.g., neutral buffered saline or phosphate buffered

saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including e.g., oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia,

- cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry
- 5 flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and
- 10 substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparation and formulations.

- Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or
- 15 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared in such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated
- 20 by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

- For oral administration the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation.
- 25 Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may
- 30 be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and  
5 U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain  
10 a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that  
15 easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable  
20 oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be  
25 preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution,  
30 the solution should be suitably buffered if necessary and the liquid diluent first rendered

isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase

“pharmaceutically-acceptable” refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles.

- 5 Methods for delivering genes, nucleic acids, and peptide compositions directly to the lungs *via* nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in  
10 the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

- In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of  
15 the present invention may be formulated for delivery either encapsulated in a lipid particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

- The formation and use of liposome and liposome-like preparations as  
20 potential drug carriers is generally known to those of skill in the art (see for example, Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998 Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent  
25 5,795,587, each specifically incorporated herein by reference in its entirety).

- Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition,  
30 liposomes are free of the DNA length constraints that are typical of viral-based delivery



systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1  $\mu\text{m}$ ) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

#### Cancer Therapeutic Methods

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of lung cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the

pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for

immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a  
5 polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented  
10 with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by  
15 intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous,  
20 intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when  
25 administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that  
30 leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or

- partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the
- 5 size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free

10 survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### 15 Cancer Detection and Diagnostic Compositions, Methods and Kits

- In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to
- 20 indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence
- 25 of a cancer. In general, a lung tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory,

1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

5 In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a  
10 binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to  
15 which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and polypeptide portions thereof to which the binding agent binds, as described above.

20 The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a  
25 magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption,  
30 and covalent attachment (which may be a direct linkage between the agent and

functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

- 10 Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an  
15 aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

- In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized  
20 on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of  
25 detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

- More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such  
30 as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The

immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as lung cancer, the signal detected from the reporter group that remains bound to the solid support is

generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site



generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25  $\mu$ g/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells,

activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

5 As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*,  
10 hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

15 To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably,  
20 oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous  
25 nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which  
5 may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as  
10 compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the  
15 level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either  
20 remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively,  
25 polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein  
30 markers may be based on routine experiments to determine combinations that results in

optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

### EXAMPLE 1

#### PREPARATION OF LUNG TUMOR-SPECIFIC CDNA SEQUENCES USING DIFFERENTIAL DISPLAY RT-PCR

This example illustrates the preparation of cDNA molecules encoding lung tumor-specific polypeptides using a differential display screen.

Tissue samples were prepared from lung tumor and normal tissue of a patient with lung cancer that was confirmed by pathology after removal of samples from the patient. Normal RNA and tumor RNA was extracted from the samples and mRNA was isolated and converted into cDNA using a (dT)<sub>12</sub>AG (SEQ ID NO: 47)

anchored 3' primer. Differential display PCR was then executed using a randomly chosen primer (SEQ ID NO: 48). Amplification conditions were standard buffer containing 1.5 mM MgCl<sub>2</sub>, 20 pmol of primer, 500 pmol dNTP and 1 unit of Taq DNA polymerase (Perkin-Elmer, Branchburg, NJ). Forty cycles of amplification were performed using 94 °C denaturation for 30 seconds, 42 °C annealing for 1 minute and 72 °C extension for 30 seconds. Bands that were repeatedly observed to be specific to the RNA fingerprint pattern of the tumor were cut out of a silver stained gel, subcloned into the pGEM-T vector (Promega, Madison, WI) and sequenced. The isolated 3' sequences are provided in SEQ ID NO: 1-16.

Comparison of these sequences to those in the public databases using the BLASTN program, revealed no significant homologies to the sequences provided in SEQ ID NO: 1-11. To the best of the inventors' knowledge, none of the isolated DNA sequences have previously been shown to be expressed at a greater level in human lung tumor tissue than in normal lung tissue.

## EXAMPLE 2

### USE OF PATIENT SERA TO IDENTIFY DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by expression screening of lung tumor samples with autologous patient sera.

A human lung tumor directional cDNA expression library was constructed employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a late SCID mouse passaged human squamous epithelial lung carcinoma and poly A+ RNA was isolated using the Message Maker kit (Gibco BRL, Gaithersburg, MD). The resulting library was screened using *E. coli*-absorbed autologous patient serum, as described in Sambrook et al., (*Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989), with the secondary antibody being goat anti-human IgG-A-M (H + L) conjugated with alkaline phosphatase, developed with NBT/BCIP (Gibco

BRL). Positive plaques expressing immunoreactive antigens were purified. Phagemid from the plaques was rescued and the nucleotide sequences of the clones was determined.

Fifteen clones were isolated, referred to hereinafter as LT86-1 – LT86-

- 5 15. The isolated cDNA sequences for LT86-1 – LT86-8 and LT86-10 - LT86-15 are provided in SEQ ID NO: 17-24 and 26-31, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 32-39 and 41-46, respectively. The determined cDNA sequence for LT86-9 is provided in SEQ ID NO: 25, with the corresponding predicted amino acid sequences from the 3' and 5' ends  
10 being provided in SEQ ID NO: 40 and 65, respectively. These sequences were compared to those in the gene bank as described above. Clones LT86-3, LT86-6 – LT86-9, LT86-11 – LT86-13 and LT86-15 (SEQ ID NO: 19, 22-25, 27-29 and 31, respectively) were found to show some homology to previously identified expressed sequence tags (ESTs), with clones LT86-6, LT86-8, LT86-11, LT86-12 and LT86-15  
15 appearing to be similar or identical to each other. Clone LT86-3 was found to show some homology with a human transcription repressor. Clones LT86-6, 8, 9, 11, 12 and 15 were found to show some homology to a yeast RNA Pol II transcription regulation mediator. Clone LT86-13 was found to show some homology with a *C. elegans* leucine aminopeptidase. Clone LT86-9 appears to contain two inserts, with the 5' sequence  
20 showing homology to the previously identified antisense sequence of interferon alpha-induced P27, and the 3' sequence being similar to LT86-6. Clone LT86-14 (SEQ ID NO: 30) was found to show some homology to the trithorax gene and has an "RGD" cell attachment sequence and a beta-Lactamase A site which functions in hydrolysis of penicillin. Clones LT86-1, LT86-2, LT86-4, LT86-5 and LT86-10 (SEQ ID NOS: 17,  
25 18, 20, 21 and 26, respectively) were found to show homology to previously identified genes. A subsequently determined extended cDNA sequence for LT86-4 is provided in SEQ ID NO: 66, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 67.

- Subsequent studies led to the isolation of five additional clones, referred  
30 to as LT86-20, LT86-21, LT86-22, LT86-26 and LT86-27. The determined 5' cDNA

sequences for LT86-20, LT86-22, LT86-26 and LT86-27 are provided in SEQ ID NO: 68 and 70-72, respectively, with the determined 3' cDNA sequences for LT86-21 being provided in SEQ ID NO: 69. The corresponding predicted amino acid sequences for LT86-20, LT86-21, LT86-22, LT86-26 and LT86-27 are provided in SEQ ID NO: 73-77, respectively. LT86-22 and LT86-27 were found to be highly similar to each other. Comparison of these sequences to those in the gene bank as described above, revealed no significant homologies to LT86-22 and LT86-27. LT86-20, LT86-21 and LT86-26 were found to show homology to previously identified genes.

In further studies, a cDNA expression library was prepared using mRNA from a lung small cell carcinoma cell line in the lambda ZAP Express expression vector (Stratagene), and screened as described above, with a pool of two lung small cell carcinoma patient sera. The sera pool was adsorbed with *E. coli* lysate and human PBMC lysate was added to the serum to block antibody to proteins found in normal tissue. Seventy-three clones were isolated. The determined cDNA sequences of these clones are provided in SEQ ID NO: 290-362. The sequences of SEQ ID NO: 289-292, 294, 296-297, 300, 302, 303, 305, 307-315, 317-320, 322-325, 327-332, 334, 335, 338-341, 343-352, 354-358, 360 and 362 were found to show some homology to previously isolated genes. The sequences of SEQ ID NO: 293, 295, 298, 299, 301, 304, 306, 316, 321, 326, 333, 336, 337, 342, 353, 359 and 361 were found to show some homology to previously identified ESTs.

### EXAMPLE 3

#### USE OF MOUSE ANTISERA TO IDENTIFY DNA SEQUENCES ENCODING

##### LUNG TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by screening of lung tumor cDNA libraries with mouse anti-tumor sera.

A directional cDNA lung tumor expression library was prepared as described above in Example 2. Sera was obtained from SCID mice containing late passaged human squamous cell and adenocarcinoma tumors. These sera were pooled and injected into normal mice to produce anti-lung tumor serum. Approximately 200,000 PFUs were screened from the unamplified library using this antiserum. Using

a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (BRL Labs.), approximately 40 positive plaques were identified. Phage was purified and phagemid excised for 9 clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

5               The determined cDNA sequences for 7 of the isolated clones (hereinafter referred to as L86S-3, L86S-12, L86S-16, L86S-25, L86S-36, L86S-40 and L86S-46) are provided in SEQ ID NO: 49-55, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 56-62, respectively. The 5' cDNA sequences for the remaining 2 clones (hereinafter referred to as L86S-30 and L86S-41) are  
10 provided in SEQ ID NO: 63 and 64. L86S-36 and L86S-46 were subsequently determined to represent the same gene. Comparison of these sequences with those in the public database as described above, revealed no significant homologies to clones L86S-30, L86S-36 and L86S-46 (SEQ ID NO: 63, 53 and 55, respectively). L86S-16 (SEQ ID NO: 51) was found to show some homology to an EST previously identified in  
15 fetal lung and germ cell tumor. The remaining clones were found to show at least some degree of homology to previously identified human genes. Subsequently determined extended cDNA sequences for L86S-12, L86S-36 and L86S-46 are provided in SEQ ID NO: 78-80, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 81-83.

20               Subsequent studies led to the determination of 5' cDNA sequences for an additional nine clones, referred to as L86S-6, L86S-11, L86S-14, L86S-29, L86S-34, L86S-39, L86S-47, L86S-49 and L86S-51 (SEQ ID NO: 84-92, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NO: 93-101, respectively. L86S-30, L86S-39 and L86S-47 were found to be similar to each other.  
25 Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to L86S-14. L86S-29 was found to show some homology to a previously identified EST. L86S-6, L86S-11, L86S-34, L86S-39, L86S-47, L86S-49 and L86S-51 were found to show some homology to previously identified genes.



In further studies, a directional cDNA library was constructed using a Stratagene kit with a Lambda Zap Express vector. Total RNA for the library was isolated from two primary squamous lung tumors and poly A+ RNA was isolated using an oligo dT column. Antiserum was developed in normal mice using a pool of sera from three SCID mice implanted with human squamous lung carcinomas. Approximately 700,000 PFUs were screened from the unamplified library with *E. coli* absorbed mouse anti-SCID tumor serum. Positive plaques were identified as described above. Phage was purified and phagemid excised for 180 clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined cDNA sequences for 23 of the isolated clones are provided in SEQ ID NO: 126-148. Comparison of these sequences with those in the public database as described above revealed no significant homologies to the sequences of SEQ ID NO: 139 and 143-148. The sequences of SEQ ID NO: 126-138 and 140-142 were found to show homology to previously identified human polynucleotide sequences.

#### EXAMPLE 4

##### USE OF MOUSE ANTISERA TO SCREEN LUNG TUMOR LIBRARIES

##### PREPARED FROM SCID MICE

This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by screening of lung tumor cDNA libraries prepared from SCID mice with mouse anti-tumor sera.

A directional cDNA lung tumor expression library was prepared using a Stratagene kit with a Lambda Zap Express vector. Total RNA for the library was taken from a late passaged lung adenocarcinoma grown in SCID mice. Poly A+ RNA was isolated using a Message Maker Kit (Gibco BRL). Sera was obtained from two SCID mice implanted with lung adenocarcinomas. These sera were pooled and injected into normal mice to produce anti-lung tumor serum. Approximately 700,000 PFUs were screened from the unamplified library with *E. coli*-absorbed mouse anti-SCID tumor serum. Positive plaques were identified with a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (Gibco BRL). Phage

was purified and phagemid excised for 100 clones with insert in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined 5' cDNA sequences for 33 of the isolated clones are provided in SEQ ID NO: 149-181. The corresponding predicted amino acid sequences for SEQ ID NO: 149, 150, 152-154, 156-158 and 160-181 are provided in SEQ ID NO: 182, 183, 186, 188-193 and 194-215, respectively. The clone of SEQ ID NO: 151 (referred to as SAL-25) was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 184 and 185. The clone of SEQ ID NO: 153 (referred to as SAL-50) was found to contain two open reading frames encoding the predicted amino acid sequences of SEQ ID NO: 187 and 216. Similarly, the clone of SEQ ID NO: 155 (referred to as SAL-66) was found to contain two open reading frames encoding the predicted amino acid sequences of SEQ ID NO: 189 and 190. Comparison of the isolated sequences with those in the public database revealed no significant homologies to the sequences of SEQ ID NO: 151, 153 and 154. The sequences of SEQ ID NO: 149, 152, 156, 157 and 158 were found to show some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 150, 155 and 159-181 were found to show homology to sequences previously identified in humans.

Using the procedures described above, two directional cDNA libraries (referred to as LT46-90 and LT86-21) were prepared from two late passaged lung squamous carcinomas grown in SCID mice and screened with sera obtained from SCID mice implanted with human squamous lung carcinomas. The determined cDNA sequences for the isolated clones are provided in SEQ ID NO: 217-237 and 286-289. SEQ ID NO: 286 was found to be a longer sequence of LT4690-71 (SEQ ID NO: 237). Comparison of these sequences with those in the public databases revealed no known homologies to the sequences of SEQ ID NO: 219, 220, 225, 226, 287 and 288. The sequences of SEQ ID NO: 218, 221, 222 and 224 were found to show some homology to previously identified sequences of unknown function. The sequence of SEQ ID NO: 236 was found to show homology to a known mouse mRNA sequence. The sequences

of SEQ ID NO: 217, 223, 227-237, 286 and 289 showed some homology to known human DNA and/or RNA sequences.

In further studies using the techniques described above, one of the cDNA libraries described above (LT86-21) was screened with *E. coli*-absorbed mouse anti-SCID tumor serum. This serum was obtained from normal mice immunized with a pool of 3 sera taken from SCID mice implanted with human squamous lung carcinomas. The determined cDNA sequences for the isolated clones are provided in SEQ ID NO: 238-285. Comparison of these sequences with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 253, 260, 277 and 285. The sequences of SEQ ID NO: 249, 250, 256, 266, 276 and 282 were found to show some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 238-248, 251, 252, 254, 255, 257-259, 261-263, 265, 267-275, 278-281, 283 and 284 were found to show some homology to previously identified DNA or RNA sequences.

The expression levels of certain of the isolated antigens in lung tumor tissues compared to expression levels in normal tissues was determined by microarray technology. The results of these studies are shown below in Table 2, together with the databank analyses for these sequences.

TABLE 2

Clone	SEQ ID NO:	Description	LT+F/N	SCC+M/N	Squa/N	Adeno/N
2LT-3	238	Unknown (KIAA0712)	2.2	3.8	3.3	-
2LT-6	239	Lactate DH B	2.3	3.8	4.1	-
2LT-22	240	Fumarate hydratase	-	3.0	-	-
2LT-26	242	CG1-39	-	-	12.8	-
2LT-31	243	ADH7	-	-	8.4	2.2
2LT-36	244	ADH7	-	2.4	2.0	-
2LT-42	245	HMG-CoA synthase	2.2	2.6	2.2	-
2LT-54	247	(Mus) ninein	-	2.1	-	-
2LT-55	248	Ubiquitin	2.2	-	2.5	2.0
2LT-57	249	Novel	2.1	2.9	2.4	-

2LT-58	250	Novel	2.3	4.0	2.9	-
2LT-59	251	Unknown KIAA0784	2.4	3.0	2.3	2.0
2LT-62	252	Nuc Pore Cmplx- ass pro TPR	-	-	-	2.1
2LT-70	256	Unknown KIAA0871	-	2.5	2.2	2.1
2LT-73	257	Mus polyadenylate- binding	-	2.0	-	-
2LT-76	259	Trans-Golgi p230	2.1	-	2.6	-
2LT-85	263	Ribosomal protein (LS29)	-	-	-	2.1
2LT-89	265	Unknown PAC212G6	-	2.0	-	-
2LT-98	268	Melanoma diff assoc pro 9	-	-	-	2.2
2LT-100	269	Mus Collagen alpha VI	-	-	-	2.1
2LT-105	271	NY-CO-7 antigen	-	3.2	-	-
2LT-108	273	Unknown RG363M04	-	3.1	-	-
2LT-124	279	Galectin-9 (secreted)	2.3	2.7	2.0	-
2LT-126	280	L1 element L1.33 p40	2.5	-	3.1	-
2LT-128	282	Novel (kappa B- ras 2)	2.3+	-	20.4	2.5
2LT-133	284	alpha II spectrin	-	2.3	-	-

LT+F/N = Lung Tumor plus Fetal tissue over Normal tissues

SC+M/N = Lung Small Cell carcinoma plus Metastatic over Normal tissues

Squa/N = Squamous lung tumor over Normal tissues

5 Aden/N = Adenocarcinoma over Normal tissues

Full-length sequencing studies on antigen 2LT-128 (SEQ ID NO: 282) resulted in the isolation of the full-length cDNA sequence provided in SEQ ID NO: 392. This amino acid sequence encoded by this full-length cDNA sequence is provided in SEQ ID NO: 393. This antigen shows 20-fold over-expression in squamous cell carcinoma and 2.5-fold over-expression in lung adenocarcinoma. This gene has been described as a potential ras oncogene (Fenwick et al. *Science*, 287:869-873, 2000).

Extended sequence information was obtained for clones 2LT-3 (SEQ ID NO:238), 2LT-26 (SEQ ID NO:242), 2LT-57 (SEQ ID NO: 249), 2LT-58 (SEQ ID NO:250), 2LT-98 (SEQ ID NO:268) and 2LT-124 (SEQ ID NO:279). The extended cDNA sequences for these clones are set forth in SEQ ID NOs:428-433, respectively, encoding the polypeptide sequences set forth in SEQ ID NOs: 434-439, respectively.

## EXAMPLE 5

### DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for representative lung tumor polypeptides were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent. First strand synthesis was carried out using 2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42°C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. 1 µl of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β-actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous tumor from 3 patients, lung adenocarcinoma, prostate tumor, colon tumor and lung tumor), and different normal tissues, including lung from four patients, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, myocardium, retina and testes. L86S-46 was found to be expressed at high levels in lung squamous tumor, colon tumor and prostate tumor, and was undetectable in the other tissues examined. L86S-5 was found to be expressed in the lung tumor samples and in 2 out of 4 normal lung samples, but not in the other normal or tumor tissues

tested. L86S-16 was found to be expressed in all tissues except normal liver and normal stomach. Using real-time PCR, L86S-46 was found to be over-expressed in lung squamous tissue and normal tonsil, with expression being low or undetectable in all other tissues examined.

5

## EXAMPLE 6

## ISOLATION OF DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

DNA sequences encoding antigens potentially involved in squamous cell lung tumor formation were isolated as follows.

A lung tumor directional cDNA expression library was constructed  
10 employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a pool of two human squamous epithelial lung carcinomas and poly A+ RNA was isolated using oligo-dT cellulose (Gibco BRL, Gaithersburg, MD). Phagemid were rescued at random and the cDNA sequences of isolated clones were determined.

15 The determined cDNA sequence for the clone SLT-T1 is provided in SEQ ID NO: 102, with the determined 5' cDNA sequences for the clones SLT-T2, SLT-T3, SLT-T5, SLT-T7, SLT-T9, SLT-T10, SLT-T11 and SLT-T12 being provided in SEQ ID NO: 103-110, respectively. The corresponding predicted amino acid sequence for SLT-T1, SLT-T2, SLT-T3, SLT-T10 and SLT-T12 are provided in SEQ  
20 ID NO: 111-115, respectively. Comparison of the sequences for SLT-T2, SLT-T3, SLT-T5, SLT-T7, SLT-T9 and SLT-T11 with those in the public databases as described above, revealed no significant homologies. The sequences for SLT-T10 and SLT-T12 were found to show some homology to sequences previously identified in humans.

The sequence of SLT-T1 was determined to show some homology to a  
25 PAC clone of unknown protein function. The cDNA sequence of SLT-T1 (SEQ ID NO: 102) was found to contain a mutator (MUT1) domain. Such domains are known to function in removal of damaged guanine from DNA that can cause A to G transversions (see, for example, el-Deiry, W.S., 1997 *Curr. Opin. Oncol.* 9:79-87; Okamoto, K. et al. 1996 *Int. J. Cancer* 65:437-41; Wu, C. et al. 1995 *Biochem. Biophys. Res. Commun.* 214:1239-45; Porter, D.W. et al. 1996 *Chem. Res. Toxicol.* 9:1375-81). SLT-T1 may  
30

thus be of use in the treatment, by gene therapy, of lung cancers caused by, or associated with, a disruption in DNA repair.

In further studies, DNA sequences encoding antigens potentially involved in adenocarcinoma lung tumor formation were isolated as follows. A human lung tumor directional cDNA expression library was constructed employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a late SCID mouse passaged human adenocarcinoma and poly A+ RNA was isolated using the Message Maker kit (Gibco BRL, Gaithersburg, MD). Phagemid were rescued at random and the cDNA sequences of isolated clones were determined.

The determined 5' cDNA sequences for five isolated clones (referred to as SALT-T3, SALT-T4, SALT-T7, SALT-T8, and SALT-T9) are provided in SEQ ID NO: 116-120, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 121-125. SALT-T3 was found to show 98% identity to the previously identified human transducin-like enhancer protein TLE2. SALT-T4 appears to be the human homologue of the mouse H beta 58 gene. SALT-T7 was found to have 97% identity to human 3-mercaptopyruvate sulfurtransferase and SALT-T8 was found to show homology to human interferon-inducible protein 1-8U. SALT-T9 shows approximately 90% identity to human mucin MUC 5B.

cDNA sequences encoding antigens potentially involved in small cell lung carcinoma development were isolated as follows. cDNA expression libraries were constructed with mRNA from the small cell lung carcinoma cell lines NCIH69, NCIH128 and DMS79 (all available from the American Type Culture Collection, Manassas, VA) employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Phagemid were rescued at random and the cDNA sequences of 27 isolated clones were determined. Comparison of the determined cDNA sequences revealed no significant homologies to the sequences of SEQ ID NO: 372 and 373. The sequences of SEQ ID NO: 364, 369, 377, 379 and 386 showed some homology to previously isolated ESTs. The sequences of the remaining 20 clones showed some homology to previously identified genes. The cDNA sequences of these clones are provided in SEQ ID NO:

363, 365-368, 370, 371, 374-376, 378, 380-385 and 387-389, wherein SEQ ID NO: 363, 366-368, 370, 375, 376, 378, 380-382, 384 and 385 are full-length sequences.

Comparison of the cDNA sequence of SEQ ID NO: 372 indicated that this clone (referred to as 128T1) is a novel member of a family of putative seven pass transmembrane proteins. Specifically, using the computer algorithm PSORT, the protein was predicted to be a type IIIA plasma membrane seven pass transmembrane protein. A genomic clone was identified in the Genbank database which contained the predicted N-terminal 58 amino acids missing from the amino acid sequence encoded by SEQ ID NO: 372. The determined full-length cDNA sequence for the 128T1 clone is provided in SEQ ID NO: 390, with the corresponding amino acid sequence being provided in SEQ ID NO: 391.

The expression levels of certain of the isolated antigens in lung tumor tissues compared to expression levels in normal tissues was determined by microarray technology. The results of these studies are shown below in Table 3, together with the databank analyses for these sequences.

TABLE 3

Clone	SEQ ID NO:	Description	LT+F/N	SCC+M/N	Squa/N	Adeno/N
DMS79-T1	363	STAT-ind inhib of cytokine	-	2.0	-	-
DMS79-T6	367	Neuronal cell death related	-	2.2	-	-
DMS79-T9	369	Novel	-	2.2	-	-
DMS79-T10	370	Ubiquitin carrier protein	-	3.9	2.2	-
DMS79-T11	371	HPV16E1 pro binding protein	-	2.1	-	-
128-T9	378	Elongation factor 1 alpha	-	2.7	-	-
128T11	380	Malate dehydrogenase	-	2.3	2.0	-
128-T12	381	Apurinic/apryrim endonuclease	-	5.4	-	-
NCIH69-	382	Sm-like protein	-	-	2.4	-



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T3		CaSm				
NCIH69-T6	384	Transcription factor BTF3a	-	2.5	-	-

LT+F/N = Lung Tumor plus Fetal tissue over Normal tissues

SC+M/N = Lung Small Cell carcinoma plus Metastatic over Normal tissues

Squa/N = Squamous lung tumor over Normal tissues

5 Aden/N = Adenocarcinoma over Normal tissues

## EXAMPLE 7

### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

## EXAMPLE 8

### ISOLATION AND CHARACTERIZATION OF DNA SEQUENCES ENCODING LUNG TUMOR

#### ANTIGENS BY T-CELL EXPRESSION CLONING

25 Lung tumor antigens may also be identified by T cell expression cloning. One source of tumor specific T cells is from surgically excised tumors from human patients.

A non-small cell lung carcinoma was minced and enzymatically digested for several hours to release tumor cells and infiltrating lymphocytes (tumor infiltrating T cells, or TILs). The cells were washed in HBSS buffer and passed over a Ficoll (100%/75%/HBSS) discontinuous gradient to separate tumor cells and lymphocytes from non-viable cells. Two bands were harvested from the interfaces; the upper band at the 75%/HBSS interface contained predominantly tumor cells, while the lower band at the 100%/75%/HBSS interface contained a majority of lymphocytes. The TILs were expanded in culture, either in 24-well plates with culture media supplemented with 10 ng/ml IL-7 and 100 U/ml IL-2, or alternatively, 24-well plates that have been pre-coated with the anti-CD3 monoclonal antibody OKT3. The resulting TIL cultures were analyzed by FACS to confirm that a high percentage were CD8+ T-cells (>90% of gated population) with only a small percentage of CD4+ cells.

In addition, non-small cell lung carcinoma cells were expanded in culture using standard techniques to establish a tumor cell line (referred to as LT391-06), which was later confirmed to be a lung carcinoma cell line by immunohistochemical analysis. This tumor cell line was transduced with a retroviral vector to express human CD80, and characterized by FACS analysis to confirm high expression levels of CD80, class I MHC and class II MHC molecules.

The ability of the TIL lines to specifically recognize autologous lung tumor was demonstrated by cytokine release assays (IFN- $\gamma$  and TNF- $\alpha$ ) as well as  $^{51}\text{Cr}$  release assays. Briefly, TIL cells from day 21 cultures were co-cultured with either autologous or allogeneic tumor cells, EBV-immortalized LCL, or control cell lines Daudi and K562, and the culture supernatant monitored by ELISA for the presence of cytokines. The TIL specifically recognized autologous tumor but not allogeneic tumor. In addition, there was no recognition of EBV-immortalized LCL or the control cell lines, indicating that the TIL lines are tumor specific and are potentially recognizing a tumor antigen presented by autologous MHC molecules.

The characterized tumor-specific TIL lines were expanded to suitable numbers for T cell expression cloning using soluble anti-CD3 antibody in culture with irradiated EBV transformed LCLs and PBL feeder cells in the presence of 20 U/ml IL-

2. Clones from the expanded TIL lines were generated by standard limiting dilution techniques. Specifically, TIL cells were seeded at 0.5 cells/well in a 96-well U bottom plate and stimulated with CD-80-transduced autologous tumor cells, EBV transformed LCL, and PBL feeder cells in the presence of 50 U/ml IL-2. The specificity of these clones for autologous tumor was confirmed by  $^{51}\text{Cr}$  microcytotoxicity and IFN- $\gamma$  bioassays.

These CTL clones were demonstrated to be HLA-B/C restricted by antibody blocking experiments. A representative CTL clone was tested on a panel of allogeneic lung carcinomas and it recognized both autologous tumor and a lung squamous cell carcinoma (936T). As the only class I MHC molecule shared among these tumors was HLA-Cw1203, this indicated that this was the restriction element used by the CTL. This finding was confirmed by the recognition of a number of allogeneic lung carcinomas transduced with a retroviral vector encoding HLA-Cw1203 by the CTL.

PolyA mRNA was prepared from a lung tumor cell line referred to as LT391-06 using Message Maker (Life Technologies; Rockville, MD). The subsequent steps involving cDNA synthesis were performed according to Life Technologies cloning manual (SuperScript Plasmid System for cDNA Synthesis and Plasmid Cloning). Modifications to the protocol were made as follows. At the adapter addition step, EcoRI-XmnI adapters (New England Biolabs; Beverly, MA) were substituted. Size fractionated cDNAs were ligated into the expression vector system HisMax A, B, C (Invitrogen; Carlsbad, CA) to optimize for protein expression in all three coding frames. Library plasmids were then aliquotted at approximately 100 CFU/well into a 96-well block for overnight liquid amplification. From these cultures, glycerol stocks were made and pooled plasmid was prepared by automated robot (Qiagen; Valencia, CA). The concentration of the plasmid DNA in each well of the library plates was determined to be approximately 150 ng/ $\mu$ l. Initial characterization of the cDNA expression library was performed by randomly sequencing 24 primary transformants and subjecting the resulting sequences to BLAST searches against available databases.

The determined cDNA sequences are provided in SEQ ID NO: 443-480, with the results of the BLAST searches being provided in Table 4.

TABLE 4

Clone	SEQ ID NO:	GenBank Accession	Description
55163	458, 459		<i>Novel in Genbank</i>
55158	452		<i>Novel in Genbank</i>
<b>Homology to known sequences with unknown function</b>			
55153	443, 444	7018516	H. sapiens mRNA; cDNA DKFZp434M035
55154	445, 446	6437562	H. sapiens Chr 22q11 PAC Clone p393
55157	450, 451	2887408	H. sapiens KIAA0417 mRNA
55165	462, 463	3970871	H. sapiens HRIHFB2122 mRNA
<b>Homology to known sequences with known function</b>			
55155	447	7677405	H. sapiens F-box protein FBS (FBS)
55156	448, 449	3929584	H. sapiens EEN pseudogene
55161	454, 455	4503350	H. sapiens DNA (cytosine-5-)-methyltransferase 1 (DNMT1)
55162	456, 457	31220	ERK1 mRNA for protein serine/threonine kinase
55164	460, 461	6677666	H. sapiens RNA-binding protein (autoantigenic) (RALY)
55166	464, 465	3249540	H. sapiens ribonuclease P protein subunit p40 (RPP40)
55167	466, 467	7657497	H. sapiens renal tumor antigen (RAGE)
55168	468, 469	2873376	H. sapiens exportin t mRNA
55169	470, 471	3135472	H. sapiens Cre binding protein-like 2 mRNA
55171	474	4759151	H. sapiens spermine synthase (SMS)
55173	476	6688148	H. sapiens partial mRNA for NICE-3 protein
55174	477, 478	531394	Human transcriptional coactivator PC4
55175	479	6563201	H. sapiens translation initiation factor eIF-2b delta subunit
55176	480	29860	hCENP-Bgene, for centromere autoantigen B (CENP-B)
<b>Homology to Ribosomal Protein</b>			
55159	453	337494	Ribosomal protein L7a (surf 3) large subunit mRNA
55170	472, 473	4506648	H.sapiens mRNA for ribosomal protein L3

Clone	SEQ ID NO:	GenBank Accession	Description
55172	475	388031	H. sapiens ribosomal protein L11

For T cell screening, approximately 80 ng of the library plasmid DNA and 80 ng of HLA-Cw1203 plasmid DNA was mixed with the lipid Fugene according to the manufacturers' instructions and transfected in duplicate into COS-7 cells. After incubation at 37 °C for 48 hours, the transfection mixture was removed and 10,000 LT391-06 CTL were added to each well in fresh media containing human serum.

The ability of T cells to recognize an antigen in the library was assessed by cytokine release after 6 hours (TNF-alpha, WEHI bio-assay) or after 24 hours (IFN-gamma, ELISA). Approximately  $2.0 \times 10^5$  clones (in plasmid pools of 100) were screened using this system in COS-7 cells. Three plasmid pools were identified (referred to as 14F10, 19A4, and 20E10) that were recognized by LT391-06 CTL. Transfection of these plasmid pools into COS-7 cells led to production of both IFN-gamma and TNF-alpha from the LT391-06 CTL at levels significantly above background. Pools 14F10, 19A4 and 20E10 were "broken down" into several hundred individual plasmid DNAs and retested. The sequences of 24 novel clones isolated from pool 14F10 are provided in SEQ ID NO: 481-511.

One plasmid (3D9) from pool 14F10, one plasmid from pool 20E10 and 5 plasmids (2A6, 2E11, 2F12, 3F4, 3H8) from pool 19A4 were capable of reconstituting T cell recognition. Sequencing of these plasmids led to the identification of a 7.8 kB cDNA insert (referred to as clone 14F10), a 2.2 kB cDNA insert (referred to as clone 19A4; SEQ ID NO:440), and a clone referred to as 20E10. The full-length cDNA sequence for 14F10 is provided in SEQ ID NO: 441. Clone 14F10 does not contain the first two "G" nucleotides found at the 5' end of 19A4, and the 3'-proximal 24 bp of 19A4 differ from the corresponding region of 14F10 (nucleotides 2145-2165). Furthermore, 3837 bp of 3' additional sequence was isolated for clone 14F10. The 5' terminal cDNA sequence (337 bp) of clone 20E10 is provided in SEQ ID NO: 442. 20E10 contains an additional 3 nucleotides (as compared to 19A4) at the 5'-most end. The additional sequence from the 5' end of clone 20E10 contains an "ATG" and

therefore appears to contain the translational start site of a novel open reading frame. BLAST search analysis against the GenBank database identified these sequences as having significant homology with a truncated human cystine/glutamate transporter gene. Unlike the published sequence, however, clones 14F10 and 19A4 contain a unique 5' terminus consisting of 181 nucleotides. This novel sequence replaces the published 5' region and results in the removal of the reported initiating methionine (start codon) and an additional two amino acids of the reported transporter protein. Therefore, the translated product of clones 14F10 and 19A4 is different than the cystine/glutamate transporter protein. Furthermore, T cell recognition of other lung tumors demonstrates that this antigen is expressed by other tumors as well.

The epitope and amino acid sequence encoded within clones 19A4 and 14F10 which reconstitutes T cell recognition of anti-LT391-06 cells were mapped as follows. Cos-7 cells were transfected with 80 ng/well HLA-Cw1203 along with titrated amounts of cDNA encoding clone 19A4, a potential open reading frame located in the unique 5' terminus of 19A4, or the open reading frame from the cystine/glutamate (Cys-Glu) transporter gene, cloned into a eukaryotic expression vector and tested for stimulation of anti-LT391-06 T cells in a TNF assay. As a positive control Cos-7 cells were co-transfected with HLA-Cw1203 and the positive plasmid clone 19A4 described above. The Cys-Glu transporter expression construct was isolated by PCR using 5' and 3' primers specific for the known ORF of the transporter with 19A4 as template. In addition, each 5' primer contained a Kozak translation initiation site and starting methionine to drive translation of the polypeptide. CTL against LT391-06 did not recognize transfectants expressing the Cys-Glu transporter construct, but did recognize transfectants expressing 19A4 and the 5' ORF from 19A4.

In subsequent experiments, Cos-7 cells were co-transfected with 80 ng/well HLA-Cw1203 along with titrated amounts of DNA of transposition mutants F10 and C12, respectively, and tested for stimulation of anti-LT391-06 T cells in a TNF assay. As a positive control, Cos-7 cells were co-transfected with HLA-Cw1203 and clones of the 5' ORF of 19A4. Transposition mutants F10 and C12 were obtained by transposon-mediated mutation of the 14F10 clone and screening for insertion site by

sequence analyses. The transposon of mutant F10 is inserted approximately 304 bp from the 5' EcoRI cloning site of the 14F10 cDNA. This mutation did not disrupt translation of the T cell epitope. By contrast, the transposon of mutant C12, which is inserted approximately 116 bp from the 5' EcoRI cloning site of the 14F10 cDNA, was found to interrupt translation of the T cell epitope. Thus the epitope in 14F10 maps between these two transposon insertion sites. The amino acid sequence of the region between the C12 and F10 transposon insertion sites is provided in SEQ ID NO: 586.

A series of 11 overlapping 16-mer and 15-mer peptides for the region shown in SEQ ID NO: 586 were prepared and tested for stimulation of anti-LT391-06 cells, as determined by cytokine release in TNF and IFN- $\gamma$  assays. Only the peptide provided in SEQ ID NO: 587 (corresponding to residues 5-20 of SEQ ID NO: 586) stimulated cytokine release. These studies demonstrate that the HLA-Cw1203 restricted epitope of the LT391-06 antigen is contained within SEQ ID NO: 587.

## EXAMPLE 9

### ISOLATION AND CHARACTERIZATION OF DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS BY PCR SUBTRACTION

This example describes the isolation and characterization of cDNA clones from a PCR subtracted expression library prepared from the human lung tumor cell line LT391-06 described above.

Tester poly A mRNA was prepared from the cell line LT391-06 as described above. Driver poly A mRNA was isolated from a human acute T cell leukemia/T lymphocyte cell line (Jurkat) which is derived from non-lung cells and is not recognized by LT391-06 reactive T cells. The subtraction was performed according to the method of Clontech (Palo Alto, CA) with the following changes: 1) a second restriction digestion reaction of cDNA was completed using a pool of enzymes (MscI, PvuII, StuI and DraI). This was in addition to, and separate from, the Clontech recommended single restriction enzyme digestion with RsaI. Each restriction digest set was treated as a separate library to ensure that the final mixed library contained overlapping fragments. Thus, the epitope recognized by the T cells should be represented on a fragment within the library and not destroyed by the presence of a

- single restriction site within it. 2) The ratio of driver to tester cDNA was increased in the hybridization steps to increase subtraction stringency. To analyze the efficiency of the subtraction, actin was PCR amplified from dilutions of subtracted, as well as unsubtracted, PCR samples. The second amplification step utilized primers that were
- 5 modified from those normally used. Three nested PCR primers were engineered to contain a cleavable EcoRI site (not utilized during cloning) that was in one of three frames. Thus, secondary amplification with these primers resulted in products that could be ligated directly into the eukaryotic expression plasmid pcDNA4His/Max-Topo (Invitrogen). This resulted in the PCR subtracted and amplified fragments being
- 10 represented in-frame somewhere within the library. Due to the mechanics of the subtraction only 50% of fragments will be in the correct orientation. The complexity and redundancy of the library was characterized by sequencing 96 randomly picked clones from the final pooled PCR subtraction expression library, referred to as LT391-06PCR. These sequences (SEQ ID NO: 512-581) were analyzed by comparison to
- 15 sequences in publicly available databases (Table 5).

TABLE 5

Clone	SEQ ID NO:	GenBank Accession	Description
57235	532		<i>Novel in Genbank</i>
57255	547		<i>Novel in Genbank</i>
57264	554		<i>Novel in Genbank</i>
<b>Homology to known sequences with unknown function</b>			
57215	518	5689540	H. sapiens mRNA for KIAA1102 protein
57223	522	2341006	Human Xq13 3' end of PAC 92E23
57227	524	7022540	H. sapiens cDNA FLJ10480 fis, clone NT2RP2000126
57238	535	6807795	H. sapiens mRNA; cDNA DKFZp761G02121
57239	536	5757546	H. sapiens clone DJ0823F17
57243	539	7023805	H. sapiens cDNA FLJ11259 fis, clone PLACE1009045
57245	540	4884472	H. sapiens mRNA; cDNA DKFZp586O2223
57267	557	6808218	H. sapiens mRNA; cDNA DKFZp434O1519
57268	558	10040400	Sequence 12 from Patent WO9954460



Clone	SEQ ID NO:	GenBank Accession	Description
57270	560	7959775	H. sapiens PRO1489 mRNA
57271	561	4500158	H. sapiens mRNA; cDNA DKFZp586B0918
57281	567	6560920	H. sapiens clone RP11- 501O7
57283	569	285962	Human mRNA for KIAA0108 gene
57285	570	7019813	H. sapiens cDNA FLJ20002 fis, clone ADKA01577
<b>Homology to known sequences with known function</b>			
57207	512	517176	H. sapiens YAP65 mRNA
57210	514	6841233	H. sapiens HSPC292 mRNA
57211	515	2606093	H. sapiens Cyr61 protein (CYR61) mRNA
57212	516	339648	Human thioredoxin (TXN) mRNA
57219	519	4504616	H. sapiens insulin- like growth factor binding protein 3 (IGFBP3)
57221	520	7274241	H. sapiens novel retinal pigment epithelial cell protein (NORPEG)
57222	521	189564	Human, plasminogen activator inhibitor- 1 gene
57228	525	4757755	H. sapiens annexin A2 (ANXA2)
57230	527	180800	Human alpha- 1 collagen type IV gene, exon 52
57232	529	6729061	H. sapiens clone RPC11- 98D12 from 7q31
57233	530	338391	Spermidine/ spermine N1- acetyltransferase
57234	531	7305302	H. sapiens NCK- associated protein 1 (NCKAP1)
57236	533	4929722	H. sapiens CGI- 127 protein
57242	538	4503558	H. sapiens epithelial membrane protein 1 (EMP1)
57248	541	183585	Human pregnancy- specific beta- glycoprotein c
57250	543	4759283	H. sapiens ubiquitin carboxyl- terminal esterase L1 (UCHL1)
57251	544	1236321	Human laminin gamma2 chain gene (LAMC2)
57253	545	213831	H. sapiens lysyl hydroxylase isoform 2 (PLOD2)
57254	546	536897	Human follistatin- related protein precursor mRNA
57257	548	339656	Human endothelial cell thrombomodulin
57258	549	190467	Human prion protein (PrP) mRNA
57261	551	338031	Human serglycin gene
57262	552	178430	Human alphoid DNA (alphoid repetitive

Clone	SEQ ID NO:	GenBank Accession	Description
			sequence)
57265	555	4502562	H. sapiens calpain, large polypeptide L2 (CAPN2)
57266	556	398163	H. sapiens mRNA for insulin- like growth factor binding protein- 3
57269	559	7262375	H. carboxylesterase 2 (intestine, liver) (CES2)
57272	562	467560	H. sapiens mRNA for cysteine dioxygenase type 1
57274	563	482664	H. sapiens annexin A3 (ANXA3)
57275	564	2281904	H. sapiens Bruton's tyr. kinase (BTK), alpha- D- galactosidase A (GLA)
57277	565	4557498	H. sapiens C- terminal binding protein 2 (CTBP2)
57282	568	189245	Human, NAD( P) H: menadiene oxidoreductase mRNA
57287	571	28525	Human mRNA for amyloid A4 precursor of Alzheimer's disease
57288	572	4757755	H. sapiens annexin A2 (ANXA2)
57289	573	5729841	H. sapiens glyoxalase I (GLO1) mRNA
57290	574	6103642	H. sapiens F- box protein FBX3 mRNA
57295	576	182513	Human ferritin L chain mRNA
57299	579	37137	Human mRNA for thrombospondin
57301	580	179682	Human (clone A12) C4b- binding protein beta- chain
57302	581	6042205	H. sapiens membrane metallo- endopeptidase (neutral endopeptidase, enkephalinase, CALLA, CD10) (MME)
57213	517	2665791	H. sapiens caveolin- 2 mRNA
57259	550	2665791	H. sapiens caveolin- 2 mRNA
57225	523	179765	Human calyccin gene
57229	526	179765	Human calyccin gene
57237	534	186962	Human laminin B2 chain gene
57249	542	186962	Human laminin B2 chain gene
57231	528	4972626	H. sapiens caveolin 1 (CAV1) gene
57296	577	4972626	H. sapiens caveolin 1 (CAV1) gene
57297	578	4972626	H. sapiens caveolin 1 (CAV1) gene
57240	537	266237	insulin- like growth factor binding protein 3
57292	575	184522	Human insulin- like growth factor- binding protein- 3 gene
57263	553	4504618	H. sapiens insulin- like growth factor

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Clone	SEQ ID NO:	GenBank Accession	Description
			binding protein 7 (IGFBP7)
57280	566	4504618	H. sapiens insulin-like growth factor binding protein 7 (IGFBP7)
<b>Homology to Ribosomal Protein</b>			
57209	513	337504	Human ribosomal protein S24 mRNA

## EXAMPLE 10

ISOLATION AND CHARACTERIZATION OF T CELL RECEPTORS FROM T CELL CLONES  
SPECIFIC FOR LUNG TUMOR ANTIGENS

5 This example describes the cloning and sequencing of T cell receptor (TCR) alpha and beta chains from a CD8 T cell clone specific for an antigen expressed by the lung tumor cell line LT391-06. T cells have a limited lifespan. Cloning of TCR chains and subsequent transfer would essentially enable infinite propagation of the T cell specificity. Cloning of tumor antigen TCR chains allows the transfer of the  
10 specificity into T cells isolated from patients that share TCR MHC-restricting alleles. Such T cells can then be expanded and used in adoptive transfer techniques to introduce the tumor antigen specificity into patients carrying tumors that express the antigen (see, for example, Clay et al. *J. Immunol.* 163:507 (1999)).

Cytotoxic T lymphocyte (CTL) clones specific for the lung tumor cell  
15 line LT391-06 were generated. Total mRNA from  $2 \times 10^6$  cells from 15 such clones was isolated using Trizol reagent and cDNA was synthesized using Ready-to-Go kits (Pharmacia). To determine Va and Vb sequences in these clones, a panel of Va and Vb subtype-specific primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of  
20 the clones expressed a common Vb sequence that corresponded to the Vb13 subfamily. Using cDNA generated from one of the clones (referred to as 1105), the Va sequence expressed was determined to be Va22. To clone the full TCR alpha and beta chains from clone 1105, primers were designed that spanned the initiator and terminator-coding TCR nucleotides. Standard 35-cycle RT-PCR reactions were established using  
25 cDNA synthesized from the CTL clone and the primers, with PWO (BMB) as the

thermostable polymerase. The resultant specific bands (approximately 850 bp for the alpha chain and approximately 950 bp for the beta chain) were ligated into the PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids containing the full-length alpha and beta chains were identified, and large  
5 scale preparations of the corresponding plasmids were generated. Plasmids containing full-length TCR alpha and beta chains were sequenced. The determined cDNA sequences for the alpha and beta chains are provided in SEQ ID NO: 583 and 582, respectively, with the corresponding amino acid sequences being provided in SEQ ID NO: 584 and 585, respectively.

10 From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

## CLAIMS

## What is Claimed:

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583;

(b) complements of the sequences provided in SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583;

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583, under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583.

2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO: 584-587;

(b) sequences encoded by a polynucleotide of claim 1; and

(c) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and

(d) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;
- (c) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO: 390, 392, 394, 396, 398-420, 422-424, 428-433 and 440-583 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;

- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 1,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.

13. A method for the treatment of a cancer in a patient, comprising administering to the patient a composition of claim 11.

14. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide according to claim 8;

(c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

15. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

16. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

17. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate;

(b) administering to the patient an effective amount of the proliferated T cells,

and thereby inhibiting the development of a cancer in the patient.



## SEQUENCE LISTING

<110> Corixa Corporation  
 Reed, Steven G.  
 Henderson, Robert A.  
 Lodes, Michael J.  
 Fling, Steven P.  
 Mohamath, Raodoh  
 Algate, Paul A.  
 Secrist, Heather  
 Indirias, Carol Yoseph  
 Benson, Darin R.  
 Elliot, Mark  
 Mannion, Jane  
 Kalos, Michael D.

<120> COMPOSITIONS AND METHODS FOR  
 THE THERAPY AND DIAGNOSIS OF LUNG CANCER

<130> 210121.47501PC

<140> PCT

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<160> 587

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&lt;212&gt; DNA

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264

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&lt;211&gt; 2624

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 19

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&lt;210&gt; 23

&lt;211&gt; 633

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 23

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&lt;210&gt; 24

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 24

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&lt;211&gt; 1758

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 25

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&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 26

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&lt;211&gt; 1331

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 27

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&lt;211&gt; 1333

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 28

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gtatggaatg	cgcttatttt	ttgaaaggat	attaggccgg	atgtgggtgc	tcacgcctgt	900
aatcccgaca	ctttgggagg	ccatggcggg	tggatcactt	gaggtcagaa	gttcaagacc	960
agcctgacca	atatgggtgaa	accccgctct	tactaaaaat	acaaaaatta	gccgggcgtg	1020
tgggcgggcg	cccatagtc	cagctactcg	ggaggctgag	acaggagact	tgcttgaacc	1080
cggggtgtgg	agggttgcct	gcagtgatta	tcatgtgttt	gcactccagc	ttggcgcgaca	1140
gagcgagact	ttgtctcaaa	aaagaagaaa	agatattatt	cccatcatga	tttcttgtga	1200
atatttgtga	tatgtcttct	gtaacctttc	ctctcccggg	cttgagcaac	ctacacactc	1260
acatgtttac	tggtagatat	gtttaaaagc	aaaataaagg	tatttgtata	aaaaaaaaaa	1320
aaaaaaactc	gag					1333

&lt;210&gt; 29

&lt;211&gt; 813

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 29

ctgagctgca	cttcagcgaa	ttcacctcgg	ctgtggctga	catgaagaac	tccttgccgg	60
accgagacaa	cagcccccagc	tcctgtgctg	gcctcttcat	tgcttcacac	atccgggttg	120
actggcccg	ggctctgggtc	caacctggaca	tcgtctgtcc	agtgcatgct	ggcgagcgag	180
ccacaggctt	tgggggtggct	ctcctactgg	ctctttttgg	ccgtgcctcc	gaggaccccg	240
tgctgaacct	ggatcccccg	ctggactgtg	agggtgaatg	ccagggaaggc	gacaaatagg	300
ggcgtgactc	caagagacgg	aggctcgtgt	gagggctact	tccacagctg	tgacacaggg	360
ttccttaoct	cattttgcac	tgactgattt	taagcaattg	aaagattaac	taactcttaa	420
gatgagttg	gottctcctt	ctgtgccccag	tggtgacagg	agtgagccat	tcttctctta	480
gaagcagctt	aggggcttgg	tggggctctg	agaaaaattg	cacagacccc	ataggtcttc	540
atctgtaagc	tctgtccctt	gtcctccacc	ctggctctta	gagccacctc	aggtcaccct	600
ctgtagttag	tgtacttctt	gacccaggcc	cttgtctcaag	ctggggctcc	ctggggtgtc	660
taaccagccc	tggttagatg	tgactggctg	ttagggaccc	cattctgtga	agcaggagac	720
cctcacagct	cccaccaacc	cccagttcac	ttgaagtgtg	atataaatg	gcccaaacat	780
aaaaaaaaaa	aaaaaaaaaa	aaaaaaactc	gag			813

&lt;210&gt; 30

&lt;211&gt; 1316

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 30

caggcgccca	gtcatggccc	aagagacagc	accaccgtgt	ggccagctct	caaggggtga	60
cagtcacaat	atagaaaaag	tggaaaaaag	gacatgtgcc	ctgtgcctgc	aaggccacga	120
gtggagtcac	ataacttttt	cccatcagg	aaatatagtt	gctcatgaaa	actgtttgct	180
gtattcatca	ggactggtgg	agtgtagagc	tcttgatcta	cgtaatacaa	ttagaacctt	240
tgatgtcaaa	tctgtaaaga	aagagatctg	gagaggaaga	agattgaaat	gctcattctg	300
taacaaagga	ggcgccacgg	tggggtgtga	tttatgggtc	tgtaagaaga	gttaccacta	360
tgctctgtgc	aaaaaggacc	aagcaattct	tcaagttgat	ggaacacctg	gaacttacaa	420
attatttttg	ccagaacatt	ctccagaaca	agaagaggcc	actgaaagtg	ctgatgacc	480
aagcatgaag	aagaagagag	gaaaaaacaa	acgcctctca	tcaggccctc	ctgcacagcc	540
aaaaacgatg	aaatgtagta	acgccaaaag	acatatgtca	gaagagacct	gtgtcacac	600
agatgcagct	gtcaaatctc	cttttcttaa	gaaatgccag	gaagcaggac	ttcttactga	660
actatttgaa	cacatactag	aaaaatatga	ttcagttcat	ggaagacttg	tggaatgagc	720
tgccctcagag	tcggactatg	aagggatcga	gaccttactg	tttgactgtg	gattatttaa	780
agacacacta	agaaaaattc	aaagaagta	caagagttaa	gctttgtaat	gggaagaaga	840
gcaaaggcag	atgaagcagc	agcttgaggc	acttgcagac	ttacaacaaa	gttgtgtctc	900
atttcaagaa	aatggggacc	tggactgtct	aagtcttaca	tcaggatcct	tgctacctcc	960
tgagagccac	cagtataaag	gtttctctag	gaaaactgga	tgggggctcc	atgttctcca	1020
aggatcgagc	aagttcttct	gcctaccctg	cccaccccg	tcaaggcgca	caacaccaga	1080
gctttgtgca	gcctttaaag	gaatcttaga	gctttctctt	cttctctcta	ctctacaga	1140
tggtctcatc	atggtctcca	ctcagtatta	ataactccat	cagcatagag	caaactcaac	1200
actgtgcatt	gcacactggt	accatgggtt	tatgtcact	atcatatcac	attgccaat	1260

tttagcacac ttaataaatg cttgtcaaaa cccaaaaaaa aaaaaaaaaa ctcgag 1316

<210> 31  
 <211> 1355  
 <212> DNA  
 <213> Homo sapien

<400> 31  
 cggcggtgga tatccgagac aatctgctgg gaatttcttg ggttgacagc tcttggatcc 60  
 ctattttgaa cagtggttagt gtccctggatt acttttcaga aagaagtaac cctttttatg 120  
 acagaacatg taataaatgaa gtggtcaaaa tgcagaggct aacattagaa cacttgaatc 180  
 agatggttgg aatcgagtac atcccttttg atgtcgaaga gccattctct ttcattcatt 240  
 ggaagcaaca gggcgagtc cctgcccagg ttatcccaact agctgattac tatatcattg 300  
 ctggagtgat ctatcaggca ccagacttgg gatcagttat aaactctaga gtgcttactg 360  
 cagtgcatgg tattcagtc gcttttggat aagctatgtc atactctga tatcatcctt 420  
 ccaaaagggtg ttgtgtggcac ttcaaagatc atgaagagca agataaagtc agacctaaag 480  
 ccaaaaggaa agaagaacca agctctattt ttcagagaca acgtgtggat gctttacttt 540  
 tagacctcag acaaaatttt ccacccaat ttgtgcagct aaagcctgga gaaaagcctg 600  
 ttccagtgga tcaaacaaag aaagaggcag aacctatacc agaactgtga aaacctgagg 660  
 agaaggagac cacaagaagt gtacaacaga cagtgaagtc taaaggcccc cctgaaaaac 720  
 ggatgagact tcagtgaag ctggacaaaa gagaagcctg gaagactcct catgctagt 780  
 atcatcacctc agtactgttg cttcttgagct ttgaagtact ttattgtaac cttcttattt 840  
 gtatggaatg cgcttatttt ttgaaaggat attaggccgg atgtggtggc tcacgcctgt 900  
 aatcccgaca ctttgggagg ccattggcggg tggatcactt gaggtcagaa gtccaagacc 960  
 agcctgacca atattggtgaa acccogtctc tactaaaaat acaaaaatta gccgggcgtg 1020  
 gtggcgggcg cccatagtcc cagctactcg ggaggctgag acaggagact tgcttgaacc 1080  
 cgggagtggtg aggttgccct gacgtgatta tcatgtgtt gcactccagc ttggcgagaca 1140  
 gaacgagact ttgtctcaaa aaaagaagaa aagattattt tcccatcatg atttcttgtg 1200  
 aatatttgtt atattgtctt tggtaacctt tctctctccc gacttgaagc aacctcacc 1260  
 actcacatgt ttactggtat atattgttta aaagcaaaat aaaggatttt gttttcccaa 1320  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa ctcgag 1355

<210> 32  
 <211> 80  
 <212> PRT  
 <213> Homo sapien

<400> 32  
 Val Ser Arg Ile Arg Gly Gly Ala Lys Lys Arg Lys Lys Lys Ser Tyr  
 1 5 10 15  
 Thr Thr Pro Lys Lys Asp Lys His Gln Arg Lys Lys Val Gln Pro Ala  
 20 25 30  
 Val Leu Lys Tyr Tyr Lys Val Asp Glu Asn Gly Lys Ile Ser Cys Leu  
 35 40 45  
 Arg Arg Glu Cys Pro Ser Asp Glu Cys Gly Ala Gly Val Phe Met Ala  
 50 55 60  
 Ser His Phe Asp Arg His Tyr Cys Gly Lys Cys Cys Leu Thr His Cys  
 65 70 75 80

<210> 33  
 <211> 130  
 <212> PRT  
 <213> Homo sapien

<400> 33  
 Glu Ile Ser Asn Glu Val Arg Lys Phe Arg Thr Leu Thr Glu Leu Ile  
 1 5 10 15  
 Leu Asp Ala Gln Glu His Val Lys Asn Pro Tyr Lys Gly Lys Lys Leu



His Thr Pro Thr Pro Asp Asp His Val Phe Arg Trp Leu Ala Tyr Ser  
 290 295 300  
 Tyr Ala Ser Thr His Arg Leu Met Thr Asp Ala Arg Arg Val Cys  
 305 310 315 320  
 His Thr Glu Asp Phe Gln Lys Glu Glu Gly Thr Val Asn Gly Ala Ser  
 325 330 335  
 Trp His Thr Val Ala Gly Ser Leu Asn Asp Phe Ser Tyr Leu His Thr  
 340 345 350  
 Asn Cys Phe Glu Leu Ser Ile Tyr Val Gly Cys Asp Lys Tyr Pro His  
 355 360 365  
 Glu Ser Glu Leu Pro Glu Glu Trp Glu Asn Asn Arg Glu Ser Leu Ile  
 370 375 380  
 Val Phe Met Glu Gln Val His Arg Gly Ile Lys Gly Ile Val Arg Asp  
 385 390 395 400  
 Leu Gln Gly Lys Gly Ile Ser Asn Ala Val Ile Ser Val Glu Gly Val  
 405 410 415  
 Asn His Asp Ile Arg Thr Ala Ser Asp Gly Asp Tyr Trp Arg Leu Leu  
 420 425 430  
 Asn Pro Gly Glu Tyr Val Val Thr Ala Lys Ala Glu Gly Phe Ile Thr  
 435 440 445  
 Ser Thr Lys Asn Cys Met Val Gly Tyr Asp Met Gly Ala Thr Arg Cys  
 450 455 460  
 Asp Phe Thr Leu Thr Lys Thr Asn Leu Ala Arg Ile Arg Glu Ile Met  
 465 470 475 480  
 Glu Thr Phe Gly Lys Gln Pro Val Ser Leu Pro Ser Arg Arg Leu Lys  
 485 490 495  
 Leu Arg Gly Arg Lys Arg Arg Gln Arg Gly  
 500 505

<210> 35  
 <211> 96  
 <212> PRT  
 <213> Homo sapien

<400> 35  
 Met Asn Gly Glu Ala Asp Cys Pro Thr Asp Leu Glu Met Ala Ala Pro  
 1 5 10 15  
 Arg Gly Gln Asp Arg Trp Ser Gln Glu Asp Met Leu Thr Leu Leu Glu  
 20 25 30  
 Cys Met Lys Asn Asn Leu Pro Ser Asn Asp Ser Ser Gln Phe Lys Thr  
 35 40 45  
 Thr Gln Thr His Met Asp Arg Glu Lys Val Ala Leu Lys Asp Phe Ser  
 50 55 60  
 Gly Asp Met Cys Lys Leu Lys Trp Val Glu Ile Ser Asn Glu Val Arg  
 65 70 75 80  
 Lys Phe Arg Thr Leu Thr Glu Leu Ile Leu Asp Thr Gln Glu His Val  
 85 90 95

<210> 36  
 <211> 129  
 <212> PRT  
 <213> Homo sapien

<400> 36  
 Gly Ile Val Val Phe Ser Leu Gly Ser Met Val Ser Glu Ile Pro Glu  
 1 5 10 15  
 Lys Lys Ala Val Ala Ile Ala Asp Ala Leu Gly Lys Ile Pro Gln Thr  
 20 25 30

```

Val Leu Trp Arg Tyr Thr Gly Thr Arg Pro Ser Asn Leu Ala Asn Asn
    35          40          45
Thr Ile Leu Val Gln Trp Leu Pro Gln Asn Asp Leu Leu Gly His Pro
    50          55          60
Met Thr Arg Ala Phe Ile Thr His Ala Ser Ser His Gly Val Asn Glu
    65          70          75          80
Ser Ile Cys Asn Gly Val Pro Met Val Met Ile Pro Leu Phe Gly Asp
    85          90          95
Gln Met Asp Asn Ala Lys Arg Arg Glu Thr Lys Gly Ala Gly Val Thr
    100          105          110
Leu Asn Val Leu Glu Met Thr Ser Glu Asp Leu Glu Asp Ala Leu Lys
    115          120          125
Ser

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<210> 37
<211> 238
<212> PRT
<213> Homo sapien

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<400> 37
Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu
  1          5          10          15
Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe
    20          25          30
Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr
    35          40          45
Leu Glu His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His
    50          55          60
Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser
    65          70          75          80
Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val
    85          90          95
Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu
    100          105          110
Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr
    115          120          125
Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His
    130          135          140
Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro
    145          150          155          160
Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu
    165          170          175          180
Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu Lys Pro Gly Glu Lys
    185          190          195
Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala Glu Pro Ile Pro Glu
    200          205          210
Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys Asn Val Gln Gln Thr
    215          220          225
Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met Arg Leu Gln
    230          235

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<210> 38
<211> 202
<212> PRT
<213> Homo sapien

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<400> 38

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Lys Gly Ser Glu Gly Glu Asn Pro Leu Thr Val Pro Gly Arg Glu Lys  
 1 5 20 25 30 35 40 45 50 55 60 65 70 75 80  
 Glu Gly Met Leu Met Gly Val Lys Pro Gly Glu Asp Ala Ser Gly Pro  
 Ala Glu Asp Leu Val Arg Arg Ser Glu Lys Asp Thr Ala Ala Val Val  
 Ser Arg Gln Gly Ser Ser Leu Asn Leu Phe Glu Asp Val Gln Ile Thr  
 Glu Pro Glu Ala Glu Pro Glu Ser Lys Ser Glu Pro Arg Pro Pro Ile  
 Ser Ser Pro Arg Ala Pro Gln Thr Arg Ala Val Lys Pro Arg Leu His  
 Pro Val Lys Pro Met Asn Ala Thr Ala Thr Lys Val Ala Asn Cys Ser  
 Leu Gly Thr Ala Thr Ile Ile Gly Glu Asn Leu Asn Asn Glu Val Met  
 Met Lys Lys Tyr Ser Pro Ser Asp Pro Ala Phe Ala Tyr Ala Gln Leu  
 Thr His Asp Glu Leu Ile Gln Leu Val Leu Lys Gln Lys Glu Thr Ile  
 Ser Lys Lys Glu Phe Gln Val Arg Glu Leu Glu Asp Tyr Ile Asp Asn  
 Leu Leu Val Arg Val Met Glu Glu Thr Pro Asn Ile Leu Arg Ile Pro  
 Thr Gln Val Gly Lys Lys Ala Gly Lys Met  
 195 200

<210> 39  
 <211> 243  
 <212> PRT  
 <213> Homo sapien

<400> 39  
 Val Asn Ala Leu Gly Ile Met Ala Ala Val Asp Ile Arg Asp Asn Leu  
 1 5 10 15  
 Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu Asn Ser  
 20 25 30  
 Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe Tyr Asp  
 35 40 45  
 Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr Leu Glu  
 50 55 60  
 His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His Ala Gln  
 65 70 75 80  
 Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser Pro Ala  
 85 90 95  
 Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val Ile Tyr  
 100 105 110  
 Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu Thr Ala  
 115 120 125  
 Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr Cys Arg  
 130 135 140  
 Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His Glu Glu  
 145 150 155 160  
 Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro Ser Ser  
 165 170 175  
 Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu Arg Gln  
 180 185 190  
 Lys Ile Ser Thr Gln Ile Cys Ala Val Asp Gln Thr Lys Lys Glu Ala



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      35              40              45
Val Arg Asn Leu Ala Gln Ser Thr Phe Pro Leu Ala Ala Gln Glu Thr
  50              55              60
Pro Gly Arg Ala Pro Ala His Ala Pro Leu Ser Ser Phe Val Pro Gly
  65              70              75              80
Val Gly Gly Arg Ser Pro Ala Ser Val Gly Ile Ser Ala Pro Gly Gly
      85              90              95
Gly Pro Ser Gly Ala Ala Ala Lys Ile Pro Leu Glu Leu Thr Gln Ser
      100              105              110
Arg Val Gln Lys Ile Trp Val Pro Val Asp His Arg Pro Ser Leu Pro
      115              120              125
Arg Ser Cys Gly Pro Lys Leu Thr Asn Ser Pro Ala Val Phe Val Met
      130              135              140
Val Gly Leu Pro Arg Pro Gly Gln Asp Leu Leu Leu His Glu Ser Leu
      145              150              155              160
Leu Ala Ala

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<210> 42
<211> 243
<212> PRT
<213> Homo sapien

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<400> 42
Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser
  1              5              10              15
Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu
      20              25              30
Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys
      35              40              45
Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile Glu
      50              55              60
Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys
      65              70              75              80
Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr
      85              90              95
Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile
      100              105              110
Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp
      115              120              125
Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp
      130              135              140
His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys
      145              150              155              160
Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala
      165              170              175
Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu
      180              185              190
Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala
      195              200              205
Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys
      210              215              220
Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met
      225              230              235              240
Arg Leu Gln

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<210> 43

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<211> 244  
 <212> PRT  
 <213> Homo sapien

<400> 43  
 Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser  
 1 5 10 15  
 Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser  
 20 25 30  
 Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val  
 35 40 45  
 Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile  
 50 55 60  
 Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg  
 65 70 75 80  
 Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr  
 85 90 95  
 Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val  
 100 105 110  
 Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe  
 115 120 125  
 Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp  
 130 135 140  
 Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala  
 145 150 155 160  
 Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp  
 165 170 175  
 Ala Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln  
 180 185 190  
 Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu  
 195 200 205  
 Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr  
 210 215 220  
 Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg  
 225 230 235 240  
 Met Arg Leu Gln

<210> 44  
 <211> 109  
 <212> PRT  
 <213> Homo sapien

<400> 44  
 Glu Leu His Phe Ser Glu Phe Thr Ser Ala Val Ala Asp Met Lys Asn  
 1 5 10 15  
 Ser Val Ala Asp Arg Asp Asn Ser Pro Ser Ser Cys Ala Gly Leu Phe  
 20 25 30  
 Ile Ala Ser His Ile Gly Phe Asp Trp Pro Gly Val Trp Val His Leu  
 35 40 45  
 Asp Ile Ala Ala Pro Val His Ala Gly Glu Arg Ala Thr Gly Phe Gly  
 50 55 60  
 Val Ala Leu Leu Leu Ala Leu Phe Gly Arg Ala Ser Glu Asp Pro Leu  
 65 70 75 80  
 Leu Asn Leu Val Ser Pro Leu Asp Cys Glu Val Asp Ala Gln Glu Gly  
 85 90 95  
 Asp Asn Met Gly Arg Asp Ser Lys Arg Arg Arg Leu Val  
 100 105

<210> 45  
 <211> 324  
 <212> PRT  
 <213> Homo sapien

<400> 45  
 Arg Arg Pro Val Met Ala Gln Glu Thr Ala Pro Pro Cys Gly Pro Val  
 1 5 10 15  
 Ser Arg Gly Asp Ser Pro Ile Ile Glu Lys Met Glu Lys Arg Thr Cys  
 20 25 30  
 Ala Leu Cys Pro Glu Gly His Glu Trp Ser Gln Ile Tyr Phe Ser Pro  
 35 40 45  
 Ser Gly Asn Ile Val Ala His Glu Asn Cys Leu Leu Tyr Ser Ser Gly  
 50 55 60  
 Leu Val Glu Cys Glu Thr Leu Asp Leu Arg Asn Thr Ile Arg Asn Phe  
 65 70 75  
 Asp Val Lys Ser Val Lys Lys Glu Ile Trp Arg Gly Arg Arg Leu Lys  
 85 90 95  
 Cys Ser Phe Cys Asn Lys Gly Gly Ala Thr Val Gly Cys Asp Leu Trp  
 100 105 110  
 Phe Cys Lys Lys Ser Tyr His Tyr Val Cys Ala Lys Lys Asp Gln Ala  
 115 120 125  
 Ile Leu Gln Val Asp Gly Asn His Gly Thr Tyr Lys Leu Phe Cys Pro  
 130 135 140  
 Glu His Ser Pro Glu Gln Glu Glu Ala Thr Glu Ser Ala Asp Asp Pro  
 145 150 155  
 Ser Met Lys Lys Lys Arg Gly Lys Asn Lys Arg Leu Ser Ser Gly Pro  
 165 170 175  
 Pro Ala Gln Pro Lys Thr Met Lys Cys Ser Asn Ala Lys Arg His Met  
 180 185 190  
 Thr Glu Glu Pro His Gly His Thr Asp Ala Ala Val Lys Ser Pro Phe  
 195 200 205  
 Leu Lys Lys Cys Gln Glu Ala Gly Leu Leu Thr Glu Leu Phe Glu His  
 210 215 220  
 Ile Leu Glu Asn Met Asp Ser Val His Gly Arg Leu Val Asp Glu Thr  
 225 230 235  
 Ala Ser Glu Ser Asp Tyr Glu Gly Ile Glu Thr Leu Leu Phe Asp Cys  
 245 250 255  
 Gly Leu Phe Lys Asp Thr Leu Arg Lys Phe Gln Glu Val Ile Lys Ser  
 260 265 270  
 Lys Ala Cys Glu Trp Glu Glu Arg Gln Arg Gln Met Lys Gln Gln Leu  
 275 280 285  
 Glu Ala Leu Ala Asp Leu Gln Gln Ser Leu Cys Ser Phe Gln Glu Asn  
 290 295 300  
 Gly Asp Leu Asp Cys Ser Ser Thr Ser Gly Ser Leu Leu Pro Pro  
 305 310 315 320  
 Glu Asp His Gln

<210> 46  
 <211> 244  
 <212> PRT  
 <213> Homo sapien

<400> 46  
 Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser  
 1 5 10 15

Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser  
 20 25  
 Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val  
 35 40 45  
 Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile  
 50 55 60  
 Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg  
 65 70 75 80  
 Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr  
 85 90 95  
 Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val  
 100 105 110  
 Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe  
 115 120 125  
 Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp  
 130 135 140  
 Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala  
 145 150 155 160  
 Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp  
 165 170 175  
 Ala Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln  
 180 185 190  
 Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu  
 195 200 205  
 Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr  
 210 215 220  
 Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg  
 225 230 235 240  
 Met Arg Leu Gln

<210> 47  
 <211> 14  
 <212> DNA  
 <213> Homo sapien

<400> 47  
 tttttttttt ttag 14

<210> 48  
 <211> 10  
 <212> DNA  
 <213> Homo sapien

<400> 48  
 cttcaacctc 10

<210> 49  
 <211> 496  
 <212> DNA  
 <213> Homo sapien

<400> 49  
 gcaccatgta ccgagcactt cggctcctcg cgcgctcgcg tccctcgtg cgggctccag 60  
 ccgagccctt agcttcggct ccggtcttg gtggcgcggc cgtgccctcg ttttgccctc 120  
 cgaacgcggc tcgaatggca agccaaaatt ccttcgggat agaatatgat acctttgggt 180  
 aactaaaggt gccaaatgat aagtattatg gcgcccagac cgtgagatct acgatgaact 240  
 ttaagattgg aggtgtgaca gaaacgatgc caaccccgat tattaagct tttggcatct 300

tgaagcgagc	ggccgctgaa	gtaaacagg	attatggtct	tgatccaaag	attgctaagt	360
caataatgaa	ggcagcgagt	gaggtagctg	aaggtaaatt	aaatgatcat	tttctctctg	420
tggtatggca	gactggatca	ggaactcaga	caaatatgaa	tgtaaatgaa	gtcattagcc	480
aatagagcaa	ttgaaa					496

<210> 50  
 <211> 499  
 <212> DNA  
 <213> Homo sapien

<400> 50						
agaaaaagtc	tatgttttgc	gaaatacaga	tccaagacaa	agacaggatg	ggcactgctg	60
gaaaagtatt	taaatgcaaa	gcagctgtgc	tttgggagca	gaagcaacc	tttccattg	120
aggaataga	agttgcccca	ccaaagacta	aagaagtctg	cattaagatt	ttggccacag	180
gaatctgtcg	cacagatgac	catgtgataa	aaggaacaat	ggtgtccaag	tttccagtga	240
ttgtgggaca	tgaggcaact	gggattgtag	agagcaattg	agaaggagtg	actacagtga	300
aaccaggtga	caaagtcatt	octctcttct	tgccacaatg	tagagaatgc	aatgcttctc	360
gcaaccacga	tggaacacct	tgcattagga	gcgatatatt	tggtcgtgga	gtactggctg	420
atggcaccac	cagattttaca	tgcaaggcg	aaccagttca	ccacttcatg	aacaccagta	480
catttacaga	gtacacagt					499

<210> 51  
 <211> 887  
 <212> DNA  
 <213> Homo sapien

<400> 51						
gagtcctgagc	agaaaggaaa	agcagccttg	gcagccacgt	tagaggaata	caaagccaca	60
ttggccaggt	accagataga	gatgaatcgc	ctgaaggctc	agctggagaa	tgaaaagcag	120
aaagtggcag	agctgtattc	tatccataac	tctggagaca	aatctgatat	tcaggacctc	180
ctggagagtg	tcaggctgga	caaagaaaaa	gcagagactt	ttgctagttag	cttcgaggaa	240
gatctggctc	atacccgaaa	tgaatgccaat	cgattacagg	atgcatttgc	taaggttagag	300
tagaataacc	gagccttcca	agaagaagct	aagaaacaaa	ttgaagattt	gaatatgacg	360
ttagaaaaat	taagatcaga	octggatgaa	aaagaaacag	aaaggagtga	catgaaagaa	420
accatctttg	aacttgaaga	tgaagtagaa	caacatcgtg	ctgtgaaact	tcattgacaac	480
ctcattattt	ctgatctaga	gaatacagtt	aaaaaaactc	aggacacaaa	gcacgacatg	540
gaaagagaaa	taaaagacat	ccacagaaga	cttcggggaag	aatctgcgga	atggcggcag	600
tttcaggctg	atctccagac	tgcatgtatc	attgcaaatg	acattaaatc	tgaaagccaa	660
gaggagattg	gtgatctaaa	gcgccggtta	catgaggctc	aagaaaaaaa	tgagaaactc	720
acaaaagaat	tgaggagaaat	aaagtcacgc	aagcaagagg	aggagcgagg	cggttataca	780
attatcatgaa	tgccgttgat	agagatttgg	cagccttaag	gcagggaatg	ggactgagta	840
gaaggtctctc	gaacttctca	agcccaactc	ctacagttaa	aaccttc		887

<210> 52  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

<400> 52						
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aaggaaacct	tcaactcttg	ggcctactac	agctctctctc	aggatttgc	ctatccagat	120
cctgtctatg	ctcagttttc	agttcagaaa	gtcactctctc	agtctgatgg	ctccagttca	180
aaagtgaag	tcaaagtctg	agtaaatgtc	catggcattt	tcagtgtgtc	cagtgcatct	240
ttagtggagg	ttcacaagtc	tgaggaaaat	gaggagccaa	tggaacagca	tcagatgaca	300
aaggaggagg	agaagatgca	agtgagccag	gaggaaaccac	atgttgaaga	gcaacagcag	360
cagacaccag	gcagaaaaata	agggcagatc	tgaagaaatg	gagactctctc	aagctggatc	420
caaggataaa	aagatggacc	aaccacccca	agccaagaag	gcaaaagtga	agaccagtac	480
ttgtgacctg	g					491

<210> 53  
 <211> 787  
 <212> DNA  
 <213> Homo sapien

<400> 53  
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 cacgtgtaac ttgcacttca agattttctga atccatatgt agtatgtttc attgtcgtcg 120  
 caggggtagt gatcctggca gtcacccatag ctctacttgt ttacttttta gcttttgatc 180  
 aaaaatctta cttttatagg agcagttttc aactcctaaa tggttgaata aatagtcagt 240  
 taaattcacc agctacacag gaatacacgga ctttgagtgg aagaattgaa tctctgatta 300  
 ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360  
 tgaggcaaga tggtagtggt gtgagagcgg atgttgtcat gaaatttcaa ttactagaa 420  
 ataacaatgg agcatcaatg aaaagcagaa ttgagtcgtg ttacgcacaa atgctgaata 480  
 actctggaac cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540  
 cagcaaatg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600  
 agagaatcct tggaggcact gaggctgagg aggggaagctg gccgtggcaa gtcagtcctg 660  
 ggctcaataa tgcccaccac tgtggaggca gctgatcaca taacatgtgg atcctgacag 720  
 cagctcactg cttcagaagc aactctaate ctcgtgactg gattgccacg tctggtattt 780  
 ccacaaac 787

<210> 54  
 <211> 386  
 <212> DNA  
 <213> Homo sapien

<400> 54  
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 gagccaatgg aaacagatca gaatgcaaag gaggaagaga agatgcaagt ggaccaggag 120  
 gaaccacatg ttgaagagca acagcagcag acaccagcag aaaataaggc agagctctgaa 180  
 gaaatggaga cctctcaagg tggatccaag gataaaaaga tggaccaacc accccaagcc 240  
 aagaaggcaa aagtgaagac cagtactgtg gacctgcca tgcagaatca gctattatgg 300  
 cagatgaca gagagatgct caactgttac attgaaaatg agggtaagat gatcatgcag 360  
 gataaactgg agaaggagcg gaatga 386

<210> 55  
 <211> 1462  
 <212> DNA  
 <213> Homo sapien

<400> 55  
 aagcagttga gtaggcagaa aaaagaacct cttcattaag gattaaaatg tataggccag 60  
 cacgtgtaac ttgcacttca agattttctga atccatatgt agtatgtttc attgtcgtcg 120  
 caggggtagt gatcctggca gtcacccatag ctctacttgt ttacttttta gcttttgatc 180  
 aaaaatctta cttttatagg agcagttttc aactcctaaa tggttgaata aatagtcagt 240  
 taaattcacc agctacacag gaatacacgga ctttgagtgg aagaattgaa tctctgatta 300  
 ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360  
 tgaggcaaga tggtagtggt gtgagagcgg atgttgtcat gaaatttcaa ttactagaa 420  
 ataacaatgg agcatcaatg aaaagcagaa ttgagtcgtg ttacgcacaa atgctgaata 480  
 actctggaac cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540  
 cagcaaatg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600  
 agagaatcct tggaggcact gaggctgagg aggggaagctg gccgtggcaa gtcagtcctg 660  
 ggctcaataa tgcccaccac tgtggaggca gctgatcaca taacatgtgg atcctgacag 720  
 cagctcactg cttcagaagc aactctaate ctcgtgactg gattgccacg tctggtattt 780  
 ccacaacatt tcctaaataa aagaatgagag taagaaatat ttaattcat aacaattata 840  
 aatctgcaac tcattgaaat gacattgcac ttgtgagact tgagaacagt gtcacattta 900  
 ccaaagatat ccatagtgtg tgtctccag ctgtaacca gaattatcca cctggctcta 960



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gagccatctt gtctggaatg ctgtgtgctg gactacctca aggtggagtg gacgcgatgc 1140
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ctgttgcaaa gtctgtatgc aggtgtgcct gtcttaaat ccaaaagctt acatttcaac 1380
tgaaaaagaa actagaaatg tctaattta acatcttgtt acataaatat gggttaacaa 1440
aaaaaaaaa aaaaaactcg ag 1462

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<210> 56
<211> 159
<212> PRT
<213> Homo sapien

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<400> 56
Thr Met Tyr Arg Ala Leu Arg Leu Leu Ala Arg Ser Arg Pro Leu Val
1 5 10 15
Arg Ala Pro Ala Ala Ala Leu Ala Ser Ala Pro Gly Leu Gly Ala
20 25 30
Ala Val Pro Ser Phe Trp Pro Pro Asn Ala Ala Arg Met Ala Ser Gln
35 40 45
Asn Ser Phe Arg Ile Glu Tyr Asp Thr Phe Gly Glu Leu Lys Val Pro
50 55 60
Asn Asp Lys Tyr Tyr Gly Ala Gln Thr Val Arg Ser Thr Met Asn Phe
65 70 75 80
Lys Ile Gly Gly Val Thr Glu Arg Met Pro Thr Pro Val Ile Lys Ala
85 90 95
Phe Gly Ile Leu Lys Arg Ala Ala Ala Glu Val Asn Gln Asp Tyr Gly
100 105 110
Leu Asp Pro Lys Ile Ala Asn Ala Ile Met Lys Ala Ala Asp Glu Val
115 120 125
Ala Glu Gly Lys Leu Asn Asp His Phe Pro Leu Val Val Trp Gln Thr
130 135 140
Gly Ser Gly Thr Gln Thr Asn Met Asn Val Asn Glu Val Ile Ser
145 150 155

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<210> 57
<211> 165
<212> PRT
<213> Homo sapien

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<400> 57
Lys Lys Ser Met Phe Ala Glu Ile Gln Ile Gln Asp Lys Asp Arg Met
1 5 10 15
Gly Thr Ala Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu
20 25 30
Gln Lys Gln Pro Phe Ser Ile Glu Glu Ile Glu Val Ala Pro Pro Lys
35 40 45
Thr Lys Glu Val Arg Ile Lys Ile Leu Ala Thr Gly Ile Cys Arg Thr
50 55 60
Asp Asp His Val Ile Lys Gly Thr Met Val Ser Lys Phe Pro Val Ile
65 70 75 80
Val Gly His Glu Ala Thr Gly Ile Val Glu Ser Ile Gly Glu Gly Val
85 90 95
Thr Thr Val Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Leu Pro Gln
100 105 110
Cys Arg Glu Cys Asn Ala Cys Arg Asn Pro Asp Gly Asn Leu Cys Ile

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115	120	125
Arg Ser Asp Ile Thr Gly Arg Gly Val Leu Ala Asp Gly Thr Thr Arg		
130	135	140
Phe Thr Cys Lys Gly Glu Pro Val His His Phe Met Asn Thr Ser Thr		
145	150	155
Phe Thr Glu Tyr Thr		160
165		

<210> 58  
 <211> 259  
 <212> PRT  
 <213> Homo sapien

<400> 58
Glu Ser Glu Gln Lys Gly Lys Ala Ala Leu Ala Ala Thr Leu Glu Glu
1 5 10 15
Tyr Lys Ala Thr Val Ala Ser Asp Gln Ile Glu Met Asn Arg Leu Lys
20 25 30
Ala Gln Leu Glu Asn Glu Lys Gln Lys Val Ala Glu Leu Tyr Ser Ile
35 40 45
His Asn Ser Gly Asp Lys Ser Asp Ile Gln Asp Leu Leu Glu Ser Val
50 55 60
Arg Leu Asp Lys Glu Lys Ala Glu Thr Leu Ala Ser Ser Leu Gln Glu
65 70 75 80
Asp Leu Ala His Thr Arg Asn Asp Ala Asn Arg Leu Gln Asp Ala Ile
85 90 95
Ala Lys Val Glu Asp Glu Tyr Arg Ala Phe Gln Glu Glu Ala Lys Lys
100 105 110
Gln Ile Glu Asp Leu Asn Met Thr Leu Glu Lys Leu Arg Ser Asp Leu
115 120 125
Asp Glu Lys Glu Thr Glu Arg Ser Asp Met Lys Glu Thr Ile Phe Glu
130 135 140
Leu Glu Asp Glu Val Glu Gln His Arg Ala Val Lys Leu His Asp Asn
145 150 155 160
Leu Ile Ile Ser Asp Leu Glu Asn Thr Val Lys Lys Leu Gln Asp Gln
165 170 175
Lys His Asp Met Glu Arg Glu Ile Lys Thr Leu His Arg Arg Leu Arg
180 185 190
Glu Glu Ser Ala Glu Trp Arg Gln Phe Gln Ala Asp Leu Gln Thr Ala
195 200 205
Val Val Ile Ala Asn Asp Ile Lys Ser Glu Ala Gln Glu Glu Ile Gly
210 215 220
Asp Leu Lys Arg Arg Leu His Glu Ala Gln Glu Lys Asn Glu Lys Leu
225 230 235 240
Thr Lys Glu Leu Glu Glu Ile Lys Ser Arg Lys Gln Glu Glu Glu Arg
245 250 255

Gly Gly Tyr

<210> 59  
 <211> 125  
 <212> PRT  
 <213> Homo sapien

<400> 59
Gly Thr Ser Phe Ser Lys Asn His Ala Ala Pro Phe Ser Lys Val Leu
1 5 10 15
Thr Phe Tyr Arg Lys Glu Pro Phe Thr Leu Glu Ala Tyr Tyr Ser Ser

20				25				30							
Pro	Gln	Asp	Leu	Pro	Tyr	Pro	Asp	Pro	Ala	Ile	Ala	Gln	Phe	Ser	Val
35				40				45							
Gln	Lys	Val	Thr	Pro	Gln	Ser	Asp	Gly	Ser	Ser	Ser	Lys	Val	Lys	Val
50				55				60							
Lys	Val	Arg	Val	Asn	Val	His	Gly	Ile	Phe	Ser	Val	Ser	Ser	Ala	Ser
65				70				75							
Leu	Val	Glu	Val	His	Lys	Ser	Glu	Glu	Asn	Glu	Glu	Pro	Met	Glu	Thr
85				90				95							
Asp	Gln	Asn	Ala	Lys	Glu	Glu	Glu	Lys	Met	Gln	Val	Asp	Gln	Glu	Glu
100				105				110							
Pro	His	Val	Glu	Glu	Gln	Gln	Gln	Thr	Pro	Gly	Arg				
115				120				125							

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<210> 60
<211> 246
<212> PRT
<213> Homo sapien
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[illegible]

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<210> 61
<211> 128
<212> PRT
<213> Homo sapien
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&lt;400&gt; 61

Gly Ile Phe Ser Val Ser Ser Ala Ser Leu Val Glu Val His Lys Ser  
 1 5 10 15  
 Glu Glu Asn Glu Glu Pro Met Glu Thr Asp Gln Asn Ala Lys Glu Glu  
 20 25 30  
 Glu Lys Met Gln Val Asp Gln Glu Glu Pro His Val Glu Glu Gln Gln  
 35 40 45  
 Gln Gln Thr Pro Ala Glu Asn Lys Ala Glu Ser Glu Glu Met Glu Thr  
 50 55 60  
 Ser Gln Ala Gly Ser Lys Asp Lys Lys Met Asp Gln Pro Pro Gln Ala  
 65 70 75 80  
 Lys Lys Ala Lys Val Lys Thr Ser Thr Val Asp Leu Pro Ile Glu Asn  
 85 90 95  
 Gln Leu Leu Trp Gln Ile Asp Arg Glu Met Leu Asn Leu Tyr Ile Glu  
 100 105 110  
 Asn Glu Gly Lys Met Ile Met Gln Asp Lys Leu Glu Lys Glu Arg Asn  
 115 120 125

&lt;210&gt; 62

&lt;211&gt; 418

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 62

Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro  
 1 5 10 15  
 Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val  
 20 25 30  
 Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr  
 35 40 45  
 Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln  
 50 55 60  
 Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile  
 65 70 75 80  
 Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln  
 85 90 95  
 Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val  
 100 105 110  
 Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly  
 115 120 125  
 Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn  
 130 135 140  
 Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu  
 145 150 155 160  
 Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly  
 165 170 175  
 Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu  
 180 185 190  
 Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn  
 195 200 205  
 Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr  
 210 215 220  
 Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala  
 225 230 235 240  
 Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg  
 245 250 255  
 Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp  
 260 265 270

Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile  
 275 280  
 His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser  
 290 295 300  
 Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr  
 305 310 315 320  
 Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val  
 325 330 335  
 Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu  
 340 345 350  
 Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser  
 355 360 365  
 Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val  
 370 375 380  
 Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly  
 385 390 395 400  
 Val Tyr Thr Arg Val Thr Ala Tyr Ile Asp Trp Ile Arg Gln Gln Thr  
 405 410 415  
 Gly Ile

<210> 63  
 <211> 776  
 <212> DNA  
 <213> Homo sapien

<400> 63  
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 aggcagtagc agtggatcgg gccaaagaagg aggcagctga gaaggaacag gaacttttaa 120  
 aacagaaatt acaggagcag ccagcaacag atggaggctc aagataagag tcgcaaggaa 180  
 aactagccaa ctgaaggaga agctgcagat ggagagagaa cacctactga gagagcagat 240  
 tatgatgttg gagcacacgc agaagggtcca aaatgattgg ctctatgaag gatttaagaa 300  
 gaagtatgag gagatgaatg cagagataag tcaattttaa cgtatgattg atactacaaa 360  
 aaatgatgat actcctcgga ttgcacgaac cttggacaac cttgccgatg agctaactgc 420  
 aatattgtct gctcctgcta aattaattgg tcatggtgtc aaagggtgta gctcaactctt 480  
 taaaaagcat aaagctccctt tttaaggata ttatagattg tacatatatg ctttggacta 540  
 tttttgatct gtatgttttt cattttcatt cagcaagttt tttttttttt tcaagtgctt 600  
 actctgttgc ccaggctgga gtacagtggg gcaactctcag ctcaactgcaa cctctgcctc 660  
 ctgggttcaa gagattcacc tgcctcagcc cctagtagc tgggattata ggtgtacacc 720  
 accacaccca gctaattttt gtatttttag tagagatggg gtttcaactat gttggc 776

<210> 64  
 <211> 160  
 <212> DNA  
 <213> Homo sapien

<400> 64  
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 gccctcagtt agcctcggcc caagaggcct gctttccact cgctagcccc gccgggggtc 120  
 cgtgtcctgt ctcgggtgcc ggaccgggc ccgagcccaa 160

<210> 65  
 <211> 72  
 <212> PRT  
 <213> Homo sapien

<400> 65  
 Leu Ser Ala Met Gly Phe Thr Ala Ala Gly Ile Ala Ser Ser Ser Ile

1	5	10	15
Ala Ala Lys Met Met Ser Ala Ala Ala Ile Ala Asn Gly Gly Gly Val			
	20	25	30
Ala Ser Gly Ser Leu Val Ala Thr Leu Gln Ser Leu Gly Ala Thr Gly			
	35	40	45
Leu Ser Gly Leu Thr Lys Phe Ile Leu Gly Ser Ile Gly Ser Ala Ile			
	50	55	60
Ala Ala Val Ile Ala Arg Phe Tyr			
65	70		

&lt;210&gt; 66

&lt;211&gt; 2581

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 66

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gctggacagc	tggaggatga	acggagaagc	cgactgcccc	acagacctg	aaatggcccg	180
ccccaagggc	caagaccggt	ggtcccgagg	agacatgctg	actttgctg	aatgcatgaa	240
gaacaacott	ccatccaatg	acagctccaa	gttcaaaacc	accgaatcac	acatggagctg	300
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ttctaatgag	gtgaggaagt	tccgtacatt	gacagaattg	atcctcgatg	ctcaggaaac	420
tgtaaaaaat	cottacaaga	gcaaaaaact	caagaaacac	ccagacttcc	caaaagaagcc	480
cctgaccctt	tatttccgct	tcttcattgga	gaagcggggc	aagtatgcga	aactccaccc	540
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gtcccagaag	gtcaggagag	cctatcacaa	gaagtgtgat	cagaaaaaga	aagattacga	1200
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ggaagagaag	atgctgaaca	tcaacaagaa	gcaggccacc	agccccgcct	ccaaagaagcc	1320
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aaattcttcc	aagaagatga	aattccaggg	agaacccaag	aagcctccca	tgaacgggta	1860
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g 2581

<210> 67  
<211> 764  
<212> PRT  
<213> Homo sapien

<400> 67  
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Cys Met Lys Asn Asn Leu Pro Ser Asn Asp Ser Ser Lys Phe Lys Thr  
35 40 45  
Thr Glu Ser His Met Asp Trp Glu Lys Val Ala Phe Lys Asp Phe Ser  
50 55 60  
Gly Asp Met Cys Lys Leu Lys Trp Val Glu Ile Ser Asn Glu Val Arg  
65 70 75 80  
Lys Phe Arg Thr Leu Thr Glu Leu Ile Leu Asp Ala Gln Glu His Val  
85 90 95  
Lys Asn Pro Tyr Lys Gly Lys Lys Leu Lys Lys His Pro Asp Phe Pro  
100 105 110  
Lys Lys Pro Leu Thr Pro Tyr Phe Arg Phe Phe Met Glu Lys Arg Ala  
115 120 125  
Lys Tyr Ala Lys Leu His Pro Glu Met Ser Asn Leu Asp Leu Thr Lys  
130 135 140  
Ile Leu Ser Lys Lys Tyr Lys Glu Leu Pro Glu Lys Lys Lys Met Lys  
145 150 155 160  
Tyr Ile Gln Asp Phe Gln Arg Glu Lys Gln Glu Phe Glu Arg Asn Leu  
165 170 175  
Ala Arg Phe Arg Glu Asp His Pro Asp Leu Ile Gln Asn Ala Lys Lys  
180 185 190  
Ser Asp Ile Pro Glu Lys Pro Lys Thr Pro Gln Gln Leu Trp Tyr Thr  
195 200 205  
His Glu Lys Lys Val Tyr Leu Lys Val Arg Pro Asp Ala Thr Thr Lys  
210 215 220  
Glu Val Lys Asp Ser Leu Gly Lys Gln Trp Ser Gln Leu Ser Asp Lys  
225 230 235 240  
Lys Arg Leu Lys Trp Ile His Lys Ala Leu Glu Gln Arg Lys Glu Tyr  
245 250 255  
Glu Glu Ile Met Arg Asp Tyr Ile Gln Lys His Pro Glu Leu Asn Ile  
260 265 270  
Ser Glu Glu Gly Ile Thr Lys Ser Thr Leu Thr Lys Ala Glu Arg Gln  
275 280 285  
Leu Lys Asp Lys Phe Asp Gly Arg Pro Thr Lys Pro Pro Pro Asn Ser  
290 295 300  
Tyr Ser Leu Tyr Cys Ala Glu Leu Met Ala Asn Met Lys Asp Val Pro  
305 310 315 320  
Ser Thr Glu Arg Met Val Leu Cys Ser Gln Gln Trp Lys Leu Leu Ser  
325 330 335  
Gln Lys Glu Lys Asp Ala Tyr His Lys Lys Cys Asp Gln Lys Lys Lys  
340 345 350  
Asp Tyr Glu Val Glu Leu Leu Arg Phe Leu Glu Ser Leu Pro Glu Glu  
355 360 365  
Glu Gln Gln Arg Val Leu Gly Glu Glu Lys Met Leu Asn Ile Asn Lys  
370 375 380  
Lys Gln Ala Thr Ser Pro Ala Ser Lys Lys Pro Ala Gln Glu Gly Gly

385					390					395				400
Lys	Gly	Gly	Ser	Glu	Lys	Pro	Lys	Arg	Pro	Val	Ser	Ala	Met	Phe Ile
				405					410				415	
Phe	Ser	Glu	Glu	Lys	Arg	Arg	Gln	Leu	Gln	Glu	Glu	Arg	Pro	Glu Leu
			420					425					430	
Ser	Glu	Ser	Glu	Leu	Thr	Arg	Leu	Leu	Ala	Arg	Met	Trp	Asn	Asp Leu
		435					440				445			
Ser	Glu	Lys	Lys	Lys	Ala	Lys	Tyr	Lys	Ala	Arg	Glu	Ala	Ala	Leu Lys
	450				455					460				
Ala	Gln	Ser	Glu	Arg	Lys	Pro	Gly	Gly	Glu	Arg	Glu	Arg	Gly	Lys
465				470					475					480
Leu	Pro	Glu	Ser	Pro	Lys	Arg	Ala	Glu	Glu	Ile	Trp	Gln	Gln	Ser Val
			485					490					495	
Ile	Gly	Asp	Tyr	Leu	Ala	Arg	Phe	Lys	Asn	Asp	Arg	Val	Lys	Ala Leu
		500						505				510		
Lys	Ala	Met	Glu	Met	Thr	Trp	Asn	Asn	Met	Glu	Lys	Lys	Glu	Lys Leu
		515					520					525		
Met	Trp	Ile	Lys	Lys	Ala	Ala	Glu	Asp	Gln	Lys	Arg	Tyr	Glu	Arg Glu
	530				535					540				
Leu	Ser	Glu	Met	Arg	Ala	Pro	Pro	Ala	Ala	Thr	Asn	Ser	Ser	Lys Lys
545				550					555					560
Met	Lys	Phe	Gln	Gly	Glu	Pro	Lys	Lys	Pro	Pro	Met	Asn	Gly	Tyr Gln
			565					570					575	
Lys	Phe	Ser	Gln	Glu	Leu	Leu	Ser	Asn	Gly	Glu	Leu	Asn	His	Leu Pro
		580					585					590		
Leu	Lys	Glu	Arg	Met	Val	Glu	Ile	Gly	Ser	Arg	Trp	Gln	Arg	Ile Ser
		595				600						605		
Gln	Ser	Gln	Lys	Glu	His	Tyr	Lys	Lys	Leu	Ala	Glu	Glu	Gln	Gln Lys
610					615					620				
Gln	Tyr	Lys	Val	His	Leu	Asp	Leu	Trp	Val	Lys	Ser	Leu	Ser	Pro Gln
625				630					635					640
Asp	Arg	Ala	Ala	Tyr	Lys	Glu	Tyr	Ile	Ser	Asn	Lys	Arg	Lys	Ser Met
			645					650					655	
Thr	Lys	Leu	Arg	Gly	Pro	Asn	Pro	Lys	Ser	Ser	Arg	Thr	Thr	Leu Gln
		660					665					670		
Ser	Lys	Ser	Glu	Ser	Glu	Glu	Asp	Asp	Glu	Glu	Asp	Glu	Asp	Asp Glu
		675					680					685		
Asp	Glu	Asp	Glu	Glu	Glu	Glu	Asp	Asp	Glu	Asn	Gly	Asp	Ser	Ser Glu
		690				695					700			
Asp	Gly	Gly	Asp	Ser	Ser	Glu	Ser	Ser	Ser	Glu	Asp	Glu	Ser	Glu Asp
705				710					715					720
Gly	Asp	Glu	Asn	Glu	Glu	Asp	Asp	Glu	Asp	Glu	Asp	Asp	Asp	Glu Asp
			725					730					735	
Asp	Asp	Glu	Asp	Glu	Asp	Asn	Glu	Ser	Glu	Gly	Ser	Ser	Ser	Ser Ser
		740					745						750	
Ser	Ser	Leu	Gly	Asp	Ser	Ser	Asp	Phe	Asp	Ser	Asn			
		755					760							

&lt;210&gt; 68

&lt;211&gt; 434

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 68

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ccaatcgcat	ctgcaaagtg	ttggcggta	atcaagagaa	cgagcagctt	atggaagact	180
atgagaagct	ggccagtgat	ctgttgaggt	ggatccgccg	caccatccca	tggtcgga	240



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atagacgcct	gcacaagccg	cccaagggtgc	aggagaaagt	ccagctggag	atcaacttta	360
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<210> 69  
 <211> 244  
 <212> DNA  
 <213> Homo sapien

<400> 69						
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ttatgtgctg	accttccctc	cactattgtc	ctgtgaccct	gccaaatccc	cctttgtgag	180
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cga						244

<210> 70  
 <211> 437  
 <212> DNA  
 <213> Homo sapien

<400> 70						
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<210> 71  
 <211> 271  
 <212> DNA  
 <213> Homo sapien

<400> 71						
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gaccaatcca	aggagggtg	caggaggagc	ttcaggtgac	cctccagggg	actaccggga	180
gttttgacaa	aaagtttgtg	gtgaactttt	cagaacagct	tcaatggaga	tgacttggcc	240
ttccacttca	accgccgtta	tgaggaagga	g			271

<210> 72  
 <211> 290  
 <212> DNA  
 <213> Homo sapien

<400> 72						
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ggagcgggat	gtcgttgagc	tgtgagcgtc	tgcggggcct	gctgcccag	ttcgatggcc	240
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<210> 73  
 <211> 144

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 73

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Lys Met Leu Asp Ala Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu
 1          5          10          15
Lys Ala Ile Met Thr Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly
 20          25          30
Ala Gln Lys Ala Glu Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala
 35          40          45
Val Asn Gln Glu Asn Glu Gln Leu Met Glu Asp Tyr Glu Lys Leu Ala
 50          55          60
Ser Asp Leu Leu Glu Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asn
 65          70          75          80
Arg Val Pro Glu Asn Thr Met His Ala Met Gln Gln Lys Leu Glu Asp
 85          90          95
Phe Arg Asp Tyr Arg Arg Leu His Lys Pro Pro Lys Val Gln Glu Lys
100          105          110
Cys Gln Leu Glu Ile Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu
115          120          125
Ser Asn Arg Pro Ala Phe Met Pro Ser Glu Gly Arg Met Val Ser Asp
130          135          140

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&lt;210&gt; 74

&lt;211&gt; 64

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 74

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Gly Ser Met Leu Val Glu Ser His His His Ser Leu Ile Ser Ser Thr
 1          5          10          15
Gln Gly His Lys His Cys Gly Arg Pro Gln Gly Pro Leu Pro Arg Lys
 20          25          30
Thr Arg Asp Leu Cys Ser Leu Val Tyr Val Leu Thr Phe Pro Pro Leu
 35          40          45
Leu Ser Cys Asp Pro Ala Lys Ser Pro Phe Val Arg Asn Thr Gln Glu
 50          55          60

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&lt;210&gt; 75

&lt;211&gt; 145

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 75

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Gly Thr Gly Ala Ser Ser Gly Thr Arg Thr Pro Asp Val Lys Ala Phe
 1          5          10          15
Leu Glu Ser Pro Trp Ser Leu Asp Pro Ala Ser Ala Ser Pro Glu Pro
 20          25          30
Val Pro His Ile Leu Ala Ser Ser Arg Gln Trp Asp Pro Ala Ser Cys
 35          40          45
Thr Ser Leu Gly Thr Asp Lys Cys Glu Ala Leu Leu Gly Leu Cys Gln
 50          55          60
Val Arg Gly Gly Leu Pro Pro Phe Ser Glu Pro Ser Ser Leu Val Pro
 65          70          75          80
Trp Pro Pro Gly Arg Ser Leu Pro Lys Ala Val Arg Pro Pro Leu Ser
 85          90          95
Trp Pro Pro Phe Ser Gln Gln Gln Thr Leu Pro Val Met Ser Gly Glu
100          105          110

```

Ala Leu Gly Trp Leu Gly Gln Ala Gly Ser Leu Ala Met Gly Ala Ala  
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 Pro Leu Gly Glu Pro Ala Lys Glu Asp Pro Met Leu Ala Gln Glu Ala  
 130 135 140  
 Gly  
 145

<210> 76  
 <211> 69  
 <212> PRT  
 <213> Homo sapien

<400> 76  
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 20 25 30  
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 35 40 45  
 Gly Leu Gln Val Thr Leu Gln Gly Thr Thr Glu Ser Phe Ala Gln Lys  
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 Phe Val Val Asn Phe  
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<210> 77  
 <211> 96  
 <212> PRT  
 <213> Homo sapien

<400> 77  
 Glu Pro Tyr Pro Glu Val Ser Arg Ile Pro Thr Val Arg Gly Cys Asn  
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 Gly Ser Leu Ser Gly Ala Leu Ser Cys Cys Glu Asp Ser Ala Gln Gly  
 20 25 30  
 Ser Gly Pro Pro Lys Ala Pro Thr Val Ala Glu Gly Pro Ser Ser Cys  
 35 40 45  
 Leu Arg Arg Asn Val Ile Ser Glu Arg Glu Arg Arg Lys Arg Met Ser  
 50 55 60  
 Leu Ser Cys Glu Arg Leu Arg Ala Leu Leu Pro Gln Phe Asp Gly Arg  
 65 70 75 80  
 Arg Glu Asp Met Ala Ser Val Leu Glu Met Ser Val Ala Ile Pro Ala  
 85 90 95

<210> 78  
 <211> 2076  
 <212> DNA  
 <213> Homo sapien

<400> 78  
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 ttgtgggaca tgaggcaact gggattgtag agagcattgg agaaggagtg actacagtga 300  
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 gcaaccacga tggcaacctt tgcattagga gcgatattac tggctgtgga gtactggctg 420  
 atggcaccac cagatttaca tgcaagggca aaccagtcca ccacttcag aacaccagta 480  
 catttaccga gtacacagtg gtggatgaat cttctgttgc taagattgat gatgcagctc 540

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tgctcagcat	catggcgctgt	aagtcagctg	gtgcatctag	gatcattggg	attgacctca	720
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cctttgaagt	tattgggcat	ctgaaacca	tgattgatgc	cotggcatcc	tgccacatga	900
acatggggac	cagcgtgggt	gtaggagttc	ctccatcage	caagatgtct	acctatgacc	960
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gagatgagt	ccccaaaata	gtgactgagt	tctggcga	gaaatttgac	ctggaocagt	1080
tgataactca	tgtcttacc	tttataaaaa	tcagtgaagg	atttgagctg	ctcaattcag	1140
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tcagtgtgaa	ctggagtttc	ctttgtgaga	gtccctcat	ctgaaatcat	gtatctgtct	1260
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<210> 79  
 <211> 2790  
 <212> DNA  
 <213> Homo sapien

<400> 79						
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aaaaactcta	cttttatag	agcagttttc	aaactcctaaa	tgttgaatat	aaatgctcagt	240
taaaattcacc	agctacacag	gaatacacgga	ctttgagctg	aagaattgaa	tctctgtatta	300
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&lt;210&gt; 80

&lt;211&gt; 1460

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 80

ctcaaacgag	ttgagttagc	agaaaaaaga	acctcttcat	taaggattaa	aatgtatagg	60
ccagcagctg	taacttcgac	ttcaagattt	ctgaatccat	atgtagtatg	tttcattgttc	120
gtcgacgggg	tagtgatcct	ggcagtcacc	atagctctac	ttgtttactt	tttagcttttt	180
gatcaaaaat	cttactttta	taggagcagt	tttcaactcc	taaatgttga	atataatagt	240
cagtttaaat	caccagctac	acaggaatac	aggactttga	gtggaagaat	tgaatctctg	300
attactaaaa	cattcaaaaga	atcaaattta	agaaatcagt	tcatacagagc	tcattgttgc	360
aaactgaggg	aagatggtag	tgggtgtgaga	gcggatggtg	tcatgaaatt	tcaattcaact	420
agaaataaca	atggagcatc	aatgaaaagc	agaattgagt	ctgtttttac	acaaatgctg	480
aaaaactctg	gaaacctgga	aaataaccct	tcaactgaga	taacatcaact	tactgaccag	540
gctgcagcaa	attggcttat	taatgaatgt	ggggccggtc	cagacctaata	aacattgtct	600
gagcagagaa	tccttggagg	cactgaggct	gaggagggaa	gctggccgtg	gcaagtcagt	660
ctggcggtca	ataatgccca	ccactgtgga	ggcagcctga	tcaataacat	gtggactctg	720
acagcagctc	actgcttcag	agcaaacctc	actgctctgt	actggattgg	cagctctggt	780
atttccacaa	catttctcaa	actaagaatg	agagtaagaa	atatttttaa	tcataacaac	840
tataaatctg	caactcatga	aaatgacatt	gcactttgtg	gaacttgagaa	cagtgctaac	900
tttaccaaa	atatccatag	tgtgtgtctc	ccagctgcta	cccagaatat	tccacctggc	960
tctactgctt	gtgtaacagg	atggggcgct	caagaatatg	ctggccacac	agttccagag	1020
ctaaagccaag	gacaggtcag	aaataaagt	aatgatgtat	gtaatgcacc	acatagttat	1080
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cgagtacagc	ctactccttg	ctggattagg	caacaaaact	ggatctatgt	caacagatgc	1320
atccctgttg	caaaagtctg	atgcaggttg	gcctgtctta	aattccaaag	ctttacattt	1380
caactgaaaa	agaaactaga	aatgtcctaa	tttaacatct	tgttacataa	atatggttta	1440
acaaaaaaaa	aaaaaaaaaa					1460

&lt;210&gt; 81

&lt;211&gt; 386

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 81

```

Met Phe Ala Glu Ile Gln Ile Gln Asp Lys Asp Arg Met Gly Thr Ala
1      5      10      15
Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu Gln Lys Gln
20      25      30
Pro Phe Ser Ile Glu Glu Ile Glu Val Ala Pro Pro Lys Thr Lys Glu
35      40      45
Val Arg Ile Lys Ile Leu Ala Thr Gly Ile Cys Arg Thr Asp Asp His
50      55      60
Val Ile Lys Gly Thr Met Val Ser Lys Phe Pro Val Ile Val Gly His
65      70      75
Glu Ala Thr Gly Ile Val Glu Ser Ile Gly Glu Gly Val Thr Thr Val
85      90      95
Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Leu Pro Gln Cys Arg Glu
100     105     110
Cys Asn Ala Cys Arg Asn Pro Asp Gly Asn Leu Cys Ile Arg Ser Asp
115     120     125
Ile Thr Gly Arg Gly Val Leu Ala Asp Gly Thr Thr Arg Phe Thr Cys
130     135     140
Lys Gly Lys Pro Val His His Phe Met Asn Thr Thr Phe Thr Glu
145     150     155
Tyr Thr Val Val Asp Glu Ser Ser Val Ala Lys Ile Asp Asp Ala Ala
165     170     175
Pro Pro Glu Lys Val Cys Leu Ile Gly Cys Gly Phe Ser Thr Gly Tyr
180     185     190
Gly Ala Ala Val Lys Thr Gly Lys Val Lys Pro Gly Ser Thr Cys Val
195     200     205
Val Phe Gly Leu Arg Gly Val Gly Leu Ser Val Ile Met Gly Cys Lys
210     215     220
Ser Ala Gly Ala Ser Arg Ile Ile Gly Ile Asp Leu Asn Lys Asp Lys
225     230     235
Phe Glu Lys Ala Met Ala Val Gly Ala Thr Glu Cys Ile Ser Pro Lys
245     250     255
Asp Ser Thr Lys Pro Ile Ser Glu Val Leu Ser Glu Met Thr Gly Asn
260     265     270
Asn Val Gly Tyr Thr Phe Glu Val Ile Gly His Leu Glu Thr Met Ile
275     280     285
Asp Ala Leu Ala Ser Cys His Met Asn Tyr Gly Thr Ser Val Val Val
290     295     300
Gly Val Pro Pro Ser Ala Lys Met Leu Thr Tyr Asp Pro Met Leu Leu
305     310     315
Phe Thr Gly Arg Thr Trp Lys Gly Cys Val Phe Gly Gly Leu Lys Ser
325     330     335
Arg Asp Asp Val Pro Lys Leu Val Thr Glu Phe Leu Ala Lys Lys Phe
340     345     350
Asp Leu Asp Gln Leu Ile Thr His Val Leu Pro Phe Lys Lys Ile Ser
355     360     365
Glu Gly Phe Glu Leu Leu Asn Ser Gly Gln Ser Ile Arg Thr Val Leu
370     375     380
Thr Phe
385

```

&lt;210&gt; 82

&lt;211&gt; 418

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

<400> 82

Met	Tyr	Arg	Pro	Ala	Arg	Val	Thr	Ser	Thr	Ser	Arg	Phe	Leu	Asn	Pro
1				5				10						15	
Tyr	Val	Val	Cys	Phe	Ile	Val	Val	Ala	Gly	Val	Val	Ile	Leu	Ala	Val
			20					25					30		
Thr	Ile	Ala	Leu	Leu	Val	Tyr	Phe	Leu	Ala	Phe	Asp	Gln	Lys	Ser	Tyr
			35				40					45			
Phe	Tyr	Arg	Ser	Ser	Phe	Gln	Leu	Leu	Asn	Val	Glu	Tyr	Asn	Ser	Gln
			50			55				60					
Leu	Asn	Ser	Pro	Ala	Thr	Gln	Glu	Tyr	Arg	Thr	Leu	Ser	Gly	Arg	Ile
65					70				75					80	
Glu	Ser	Leu	Ile	Thr	Lys	Thr	Phe	Lys	Glu	Ser	Asn	Leu	Arg	Asn	Gln
				85					90				95		
Phe	Ile	Arg	Ala	His	Val	Ala	Lys	Leu	Arg	Gln	Asp	Gly	Ser	Gly	Val
			100					105					110		
Arg	Ala	Asp	Val	Val	Met	Lys	Phe	Gln	Phe	Thr	Arg	Asn	Asn	Asn	Gly
			115				120					125			
Ala	Ser	Met	Lys	Ser	Arg	Ile	Glu	Ser	Val	Leu	Arg	Gln	Met	Leu	Asn
			130				135					140			
Asn	Ser	Gly	Asn	Leu	Glu	Ile	Asn	Pro	Ser	Thr	Glu	Ile	Thr	Ser	Leu
145				150						155					160
Thr	Asp	Gln	Ala	Ala	Ala	Asn	Trp	Leu	Ile	Asn	Glu	Cys	Gly	Ala	Gly
			165					170						175	
Pro	Asp	Leu	Ile	Thr	Leu	Ser	Glu	Gln	Arg	Ile	Leu	Gly	Gly	Thr	Glu
			180					185					190		
Ala	Glu	Glu	Gly	Ser	Trp	Pro	Trp	Gln	Val	Ser	Leu	Arg	Leu	Asn	Asn
			195				200					205			
Ala	His	His	Cys	Gly	Gly	Ser	Leu	Ile	Asn	Asn	Met	Trp	Ile	Leu	Thr
			210			215					220				
Ala	Ala	His	Cys	Phe	Arg	Ser	Asn	Ser	Asn	Pro	Arg	Asp	Trp	Ile	Ala
225				230						235					240
Thr	Ser	Gly	Ile	Ser	Thr	Thr	Phe	Pro	Lys	Leu	Arg	Met	Arg	Val	Arg
			245						250					255	
Asn	Ile	Leu	Ile	His	Asn	Asn	Tyr	Lys	Ser	Ala	Thr	His	Glu	Asn	Asp
			260					265					270		
Ile	Ala	Leu	Val	Arg	Leu	Glu	Asn	Ser	Val	Thr	Phe	Thr	Lys	Asp	Ile
			275				280					285			
His	Ser	Val	Cys	Leu	Pro	Ala	Ala	Thr	Gln	Asn	Ile	Pro	Pro	Gly	Ser
			290			295					300				
Thr	Ala	Tyr	Val	Thr	Gly	Trp	Gly	Ala	Gln	Glu	Tyr	Ala	Gly	His	Thr
305				310						315				320	
Val	Pro	Glu	Leu	Arg	Gln	Gly	Gln	Val	Arg	Ile	Ile	Ser	Asn	Asp	Val
			325					330					335		
Cys	Asn	Ala	Pro	His	Ser	Tyr	Asn	Gly	Ala	Ile	Leu	Ser	Gly	Met	Leu
			340					345					350		
Cys	Ala	Gly	Val	Pro	Gln	Gly	Gly	Val	Asp	Ala	Cys	Gln	Gly	Asp	Ser
			355				360					365			
Gly	Gly	Pro	Leu	Val	Gln	Glu	Asp	Ser	Arg	Arg	Leu	Trp	Phe	Ile	Val
			370			375					380				
Gly	Ile	Val	Ser	Trp	Gly	Asp	Gln	Cys	Gly	Leu	Pro	Asp	Lys	Pro	Gly
385				390						395				400	
Val	Tyr	Thr	Arg	Val	Thr	Ala	Tyr	Leu	Asp	Trp	Ile	Arg	Gln	Gln	Thr
			405						410					415	

Gly Ile

&lt;210&gt; 83

<211> 418  
 <212> PRT  
 <213> Homo sapien

<400> 83  
 Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro  
 1 5 10 15  
 Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val  
 20 25 30  
 Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr  
 35 40 45  
 Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln  
 50 55 60  
 Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile  
 65 70 75 80  
 Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln  
 85 90 95  
 Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val  
 100 105 110  
 Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly  
 115 120 125  
 Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn  
 130 135 140  
 Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu  
 145 150 155 160  
 Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly  
 165 170 175  
 Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu  
 180 185 190  
 Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn  
 195 200 205  
 Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr  
 210 215 220  
 Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala  
 225 230 235 240  
 Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg  
 245 250 255  
 Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp  
 260 265 270  
 Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile  
 275 280 285  
 His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser  
 290 295 300  
 Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr  
 305 310 315 320  
 Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val  
 325 330 335  
 Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu  
 340 345 350  
 Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser  
 355 360 365  
 Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val  
 370 375 380  
 Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly  
 385 390 395 400  
 Val Tyr Thr Arg Val Thr Ala Tyr Leu Asp Trp Ile Arg Gln Gln Thr  
 405 410 415  
 Gly Ile



<210> 84  
 <211> 489  
 <212> DNA  
 <213> Homo sapien

<400> 84  
 aaaaggggttaa gctttagatgat taccaggaac gaatgaacaa aggggaaagg cttaaatcaag 60  
 atcagcttgga tgccgtttct aagtaccagg aagtcacaaa taatttggag ttgtgcaaaag 120  
 aattacagag gagtttcatg gcaactaagtc aagatattca gaaaacaata aagaagacag 180  
 cagctcgga gcagccttatg agagaagaag ctgaacagaa acgtttaaaa actgtacttg 240  
 agctacagta tgttttggac aaattgggag atgatgaagt gcggactgac ctgaaacaag 300  
 gtttgaatgg agtgccaata ttgtccgaag aggagttgtc attgttggat gaattctata 360  
 agctagtaga ccctgaacgg gacatgagct tgagggtttaa tgaacagtat gaacatgctc 420  
 ccattcacct gtgggacctg ctggaaggga aggaaaaacc tgtatgtgga accacctata 480  
 aagttctaa 489

<210> 85  
 <211> 304  
 <212> DNA  
 <213> Homo sapien

<400> 85  
 gggacctgga ggagccacg ctgcagcatg aagccacagc agccaccctg aggaagaagc 60  
 acgcgacag cgtgcccag ctgcgggagc agatogacaa cctgcacgag gtgaagcaga 120  
 agctggagaa ggagaagagc gagatgaaga tggagatcga tgacctcgct tgtaacatgg 180  
 aggtcatctc caaatctaag ggaacacctg agaagatgtg ccgcacactg gaggaccaag 240  
 tgagttagct gaagaccagc gaggaggaac agcagcgctt gatcaatgaa ctgactgcgc 300  
 agag 304

<210> 86  
 <211> 296  
 <212> DNA  
 <213> Homo sapien

<400> 86  
 gaaaatcctt cctttgaatg ggaatctcca agcagttgaa ttgggcaaaa aaagaacctc 60  
 ttccctaaag attaaaaagt ttaggccaac acgtgttact tccacttcca gattttctgaa 120  
 tccatagtgt gtatgtttcc ttgtcctccc aggggtttgt atcctggcag tccccatagc 180  
 tctacttgtt tactttttag cttttgatca aaaatcttac tttttattga gcaattttcc 240  
 actcccaaat gttgaatata atagtccgtt taattccccc gcttcaccgg gaattc 296

<210> 87  
 <211> 904  
 <212> DNA  
 <213> Homo sapien

<400> 87  
 gtgtccagga aacgattcat gaacataaca agcttgctgc aaattcagat catctcatgc 60  
 agattcaaaa atgtgagttg gtcttgcac acacctacc agttggtgaa gacagccttg 120  
 tatctgatcg tcttaaaaaa gagttgtccc caggttttaac cagtgaagtt catagtgttc 180  
 gtgcaggacg gcatcttgct accaaattga atattttagt acagcaacat ttgactttgc 240  
 cttcaactac tattcaaat attccaatga aggaagaaca catctgtaac acatctgcga 300  
 attatgatgt ggagctactt catcacaagg atgcacatgt agattttcctg aaaagtgggtg 360  
 attcgcatct aggtggcggc agtcgagaag gctcgtttaa agaaacaata acattaaagt 420  
 ggtgtacacc aaggacaaat aacattgaat tacactattg tactggagct tatcgggatt 480  
 cacctgtaga tgtaaatagt agaccttct cctgccttac taattttctt ctaaatggtc 540

gttctgtttt	attggaacaa	ccacgaaagt	caggttctaa	agtcattagt	catatgctta	600
gtagccatgg	aggagagatt	tttttgcacg	tccttagcag	ttctcgatcc	attctagaag	660
atccaccttc	aattagttaa	ggatgtggag	gaagagttaa	agactaccgg	attacagatt	720
tttgtgaatt	tataggggga	aaacagatta	actccttttc	tacaccccgag	atataaaatc	780
gatggaagtc	ttgaggtccc	tttggaaaccg	agccaaaaga	tcagttaaaac	aaacataacc	840
gttactggcc	tatgatttca	aaaaccacc	atttttaaca	tgcaagcggg	agttccggtta	900
acca						904

&lt;210&gt; 88

&lt;211&gt; 387

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 88

cgtctctccc	ccagtttgcc	gttccaccgg	agcgctcggg	acttgcgat	agtggtgacg	60
gcggcaacat	gtctgtggct	ttcggggccc	cgaggcagcg	aggcaagggg	gagatcaotc	120
ccgctgcgat	tcagaagatg	ttggatgaca	ataacctct	tattcagttg	ataatggact	180
ctcagaataa	aggaaagacc	tcagagtgtt	ctcagtatca	gcagatgttg	cacacaaact	240
tggtatacct	tgctacaata	gcagattcta	atcaaaaata	gcagttctct	ttaccagcac	300
caccacaca	gaatatgcct	atgggtcctg	gagggatgaa	tcagagcggg	cctccccacc	360
ctccacgctc	tcacaacatg	cttccaa				387

&lt;210&gt; 89

&lt;211&gt; 481

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 89

tgttcttggg	cctgcggtgc	tatagagcag	gctcttctag	gttgccagtt	gccattggaat	60
ctggaccacaa	aattgtggcc	cccggttgcc	tggtggaaaa	taacaatgag	cagctatttg	120
tgaaaccagca	agctatacag	attcttgaaa	agattttctca	gccagtggtg	gtggtggcca	180
ttgtaggact	tgaccgtaca	gggaaatcct	acttgatgaa	ccatctggca	ggacagaatc	240
atggcttccc	ctcgggtccc	acgggtgcagt	ctgaaaccaa	gggcatctgg	atgtggtcgg	300
tgccccaccc	atccaagcca	aaccacaccc	tggtccttct	ggacacggaa	ggtctggcgg	360
atgtggaaaa	gggtgacctt	aagaatgact	cctggatctt	tgccctggct	gtgctcctgt	420
gcagcacctt	tgcttacaac	agcatgagca	ccatcaacca	ccaggccctg	gagcagctgc	480
a						481

&lt;210&gt; 90

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 90

tgaaaactgt	tcttggacct	gcggtgctat	agagcaggtt	ggcagttgcc	atggaatctg	60
gaccocaaat	gttggccccc	gtttgcctgg	tggaaaaata	caatgagcag	ctattggtga	120
accagcaagc	tatacagatt	cttgaataa	ttttctcagc	agtgtgtgtg	gtggccattg	180
taggactgta	cgttacaggg	aaatcctact	tgatgaacca	tctggcagga	cagaatcatg	240
gcttccctct	gggtccacag	gtgcagttct	aaaccaaggg	catctggatg	tggtgcgtgc	300
cccaccatc	caagccaaac	cacaccctgg	tccttctgga	caacgaaggt	ctggcgatg	360
tggaataagg	tgaccctaa	aatgactcct	ggatctttgc	cctggctgtg	ctcctgtgca	420
gcacctttgt	ctacaacagc	atgagcacca	tcaaccacca	agccctggag	cagctgcatt	480
atgtgacgga	c					491

&lt;210&gt; 91

&lt;211&gt; 488

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

```

<400> 91
ttcgacagtc agccgcacatct tcttttgcgt cgccagccga gccacatcgc tcagacacca      60
tggggaaggt gaaggtcggga gtcaacggat ttggtcgtat tggggcgctg gtcaccaggg      120
ctgcttttaa ctctggtaaa gtggatattg ttgccatcaa tgacccttc attgacctca      180
actacatggt ttacatgttc caatatgatt ccacccatgg caaattccat ggcaccgtcg      240
aggctgagaa cgggaagcgt gtcatcaatg gaaatcccat caccatcttc caggagcgag      300
atccctccaa aatcaagtgg ggcatgctg gcgctgagta cgtcgtggag tccactggcg      360
tcttcaccac catggagaag gctggggctc atttgacggg gggagccaaa agggctcatca      420
tctctgcccc tctgctgatg ccccatgttc gtcatgggtg tgaacctga gaagtatgac      480
acagcctc

```

```

<210> 92
<211> 384
<212> DNA
<213> Homo sapien

```

```

<400> 92
gacagtcagc cgcacatctct tttgcgtcgc cagccgagcc acatcgctca gacaccatgg      60
ggaaggtgaa ggtcggagtc aacggatttg gtctgattgg gcgcctggtc accagggtcg      120
cttttaactc tggtaaaagt gatattgttg ccatcaatga ccccttcatt gacctcaact      180
catggtttaa catgttccaa tatgattcca ccatggcaca attccatggc accgtcgagg      240
ctgagaacgg gaagcttgct atcaatggaa atcccatcac catcttccag gaggcgatc      300
cctccaaaat caagtggggc gatactggcg ctgagtacgt cgtggagtcg actggcgtct      360
tcaccacat ggagaaggct gggg

```

```

<210> 93
<211> 162
<212> PRT
<213> Homo sapien

```

```

<400> 93
Lys Gly Lys Leu Asp Asp Tyr Gln Glu Arg Met Asn Lys Gly Glu Arg
1      5      10
Leu Asn Gln Asp Gln Leu Asp Ala Val Ser Lys Tyr Gln Glu Val Thr
20     25     30
Asn Asn Leu Glu Phe Ala Lys Glu Leu Gln Arg Ser Phe Met Ala Leu
35     40     45
Ser Gln Asp Ile Gln Lys Thr Ile Lys Lys Thr Ala Arg Arg Glu Gln
50     55     60
Leu Met Arg Glu Glu Ala Glu Gln Lys Arg Leu Lys Thr Val Leu Glu
65     70     75     80
Leu Gln Tyr Val Leu Asp Lys Leu Gly Asp Asp Glu Val Arg Thr Asp
85     90     95
Leu Lys Gln Gly Leu Asn Gly Val Pro Ile Leu Ser Glu Glu Glu Leu
100    105    110
Ser Leu Leu Asp Glu Phe Tyr Lys Leu Val Asp Pro Glu Arg Asp Met
115    120    125
Ser Leu Arg Leu Asn Glu Gln Tyr Glu His Ala Ser Ile His Leu Trp
130    135    140
Asp Leu Leu Glu Gly Lys Glu Lys Pro Val Cys Gly Thr Thr Tyr Lys
145    150    155    160
Val Leu

```

```

<210> 94
<211> 100
<212> PRT

```

&lt;213&gt; Homo sapien

&lt;400&gt; 94

```

Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala Thr Ala Ala Thr Leu
 1          5          10          15
Arg Lys Lys His Ala Asp Ser Val Ala Glu Leu Gly Glu Gln Ile Asp
 20          25          30
Asn Leu Gln Arg Val Lys Gln Lys Leu Glu Lys Glu Lys Ser Glu Met
 35          40          45
Lys Met Glu Ile Asp Asp Leu Ala Cys Asn Met Glu Val Ile Ser Lys
 50          55          60
Ser Lys Gly Asn Leu Glu Lys Met Cys Arg Thr Leu Glu Asp Gln Val
 65          70          75          80
Ser Glu Leu Lys Thr Gln Glu Glu Glu Gln Arg Leu Ile Asn Glu
 85          90          95
Leu Thr Ala Gln
 100

```

&lt;210&gt; 95

&lt;211&gt; 99

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 95

```

Lys Ile Leu Pro Leu Asn Gly Asn Leu Gln Ala Val Glu Leu Gly Glu
 1          5          10          15
Lys Arg Thr Ser Ser Leu Arg Ile Lys Met Phe Arg Ala Thr Arg Val
 20          25          30
Thr Ser Thr Ser Arg Phe Leu Asn Pro Tyr Val Val Cys Phe Leu Val
 35          40          45
Leu Pro Gly Val Val Ile Leu Ala Val Pro Ile Ala Leu Leu Val Tyr
 50          55          60
Phe Leu Ala Phe Asp Gln Lys Ser Tyr Phe Tyr Trp Ser Asn Phe Pro
 65          70          75          80
Leu Pro Asn Val Glu Tyr Asn Ser Pro Phe Asn Ser Pro Ala Ser Pro
 85          90          95
Gly Ile Pro

```

&lt;210&gt; 96

&lt;211&gt; 257

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 96

```

Val Gln Glu Thr Ile His Glu His Asn Lys Leu Ala Ala Asn Ser Asp
 1          5          10          15
His Leu Met Gln Ile Gln Lys Cys Glu Leu Val Leu Ile His Thr Tyr
 20          25          30
Pro Val Gly Glu Asp Ser Leu Val Ser Asp Arg Ser Lys Lys Glu Leu
 35          40          45
Ser Pro Val Leu Thr Ser Glu Val His Ser Val Arg Ala Gly Arg His
 50          55          60
Leu Ala Thr Lys Leu Asn Ile Leu Val Gln Gln His Phe Asp Leu Ala
 65          70          75          80
Ser Thr Thr Ile Thr Asn Ile Pro Met Lys Glu Glu Gln His Ala Asn
 85          90          95
Thr Ser Ala Asn Tyr Asp Val Glu Leu Leu His His Lys Asp Ala His

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          100                      105                      110
Val Asp Phe Leu Lys Ser Gly Asp Ser His Leu Gly Gly Gly Ser Arg
      115                      120                      125
Glu Gly Ser Phe Lys Glu Thr Ile Thr Leu Lys Trp Cys Thr Pro Arg
      130                      135                      140
Thr Asn Asn Ile Glu Leu His Tyr Cys Thr Gly Ala Tyr Arg Ile Ser
      145                      150                      155
Pro Val Asp Val Asn Ser Arg Pro Ser Ser Cys Leu Thr Asn Phe Leu
      165                      170                      175
Leu Asn Gly Arg Ser Val Leu Leu Glu Gln Pro Arg Lys Ser Gly Ser
      180                      185                      190
Lys Val Ile Ser His Met Leu Ser Ser His Gly Gly Glu Ile Phe Leu
      195                      200                      205
His Val Leu Ser Ser Ser Arg Ser Ile Leu Glu Asp Pro Pro Ser Ile
      210                      215                      220
Ser Glu Gly Cys Gly Gly Arg Val Thr Asp Tyr Arg Ile Thr Asp Phe
      225                      230                      235
Gly Glu Phe Met Arg Gly Lys Gln Ile Asn Ser Phe Ser Thr Pro Gln
      245                      250                      255
Ile

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<210> 97
<211> 128
<212> PRT
<213> Homo sapien

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```

<400> 97
Ser Leu Pro Gln Phe Ala Val His Pro Glu Arg Ser Gly Leu Ala Asp
 1      5      10      15
Ser Gly Asp Gly Gly Asn Met Ser Val Ala Phe Ala Ala Pro Arg Gln
      20      25      30
Arg Gly Lys Gly Glu Ile Thr Pro Ala Ala Ile Gln Lys Met Leu Asp
      35      40      45
Asp Asn Asn His Leu Ile Gln Cys Ile Met Asp Ser Gln Asn Lys Gly
      50      55      60
Lys Thr Ser Glu Cys Ser Gln Tyr Gln Gln Met Leu His Thr Asn Leu
      65      70      75      80
Val Tyr Leu Ala Thr Ile Ala Asp Ser Asn Gln Asn Met Gln Ser Leu
      85      90      95
Leu Pro Ala Pro Pro Thr Gln Asn Met Pro Met Gly Pro Gly Gly Met
      100     105     110
Asn Gln Ser Gly Pro Pro Pro Pro Pro Arg Ser His Asn Met Pro Ser
      115     120     125

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<210> 98
<211> 159
<212> PRT
<213> Homo sapien

```

```

<400> 98
Phe Leu Asp Leu Arg Cys Tyr Arg Ala Gly Ser Ser Arg Leu Ala Val
 1      5      10      15
Ala Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu
      20      25      30
Asn Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu
      35      40      45
Glu Lys Ile Ser Gln Pro Val Val Val Val Ala Ile Val Gly Leu Tyr

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      50              55              60
Arg Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His
65              70              75              80
Gly Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp
      85              90              95
Met Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu
      100              105              110
Leu Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn
      115              120              125
Asp Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val
      130              135              140
Tyr Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu
145              150              155

```

```

<210> 99
<211> 147
<212> PRT
<213> Homo sapien

```

```

<400> 99
Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu Asn
1              5              10              15
Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu Glu
      20              25              30
Lys Ile Ser Gln Pro Val Val Val Val Ala Ile Val Gly Leu Tyr Arg
      35              40              45
Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His Gly
50              55              60
Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp Met
65              70              75              80
Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu Leu
      85              90              95
Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn Asp
      100              105              110
Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val Tyr
      115              120              125
Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu His Tyr
130              135              140
Val Thr Asp
145

```

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<210> 100
<211> 124
<212> PRT
<213> Homo sapien

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```

<400> 100
Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg
1              5              10              15
Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile Val Ala
      20              25              30
Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln
      35              40              45
Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Glu Ala Glu Asn
50              55              60
Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg
65              70              75              80
Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val

```

85								90				95			
Glu	Ser	Thr	Gly	Val	Phe	Thr	Thr	Met	Glu	Lys	Ala	Gly	Ala	His	Leu
			100					105					110		
Gln	Gly	Gly	Ala	Lys	Arg	Val	Ile	Ile	Ser	Ala	Pro				
		115					120								

```
<210> 101
<211> 127
<212> PRT
<213> Homo sapien
```

<400> 101															
Gln	Ser	Ala	Ala	Ser	Ser	Phe	Ala	Ser	Pro	Ala	Glu	Pro	His	Arg	Ser
1				5				10					15		
Asp	Thr	Met	Gly	Lys	Val	Lys	Val	Gly	Val	Asn	Gly	Phe	Gly	Arg	Ile
			20					25					30		
Gly	Arg	Leu	Val	Thr	Arg	Ala	Ala	Phe	Asn	Ser	Gly	Lys	Val	Asp	Ile
		35					40					45			
Val	Ala	Ile	Asn	Asp	Pro	Phe	Ile	Asp	Leu	Asn	Tyr	Met	Val	Tyr	Met
		50				55					60				
Phe	Gln	Tyr	Asp	Ser	Thr	His	Gly	Lys	Phe	His	Gly	Thr	Val	Glu	Ala
65					70					75					80
Glu	Asn	Gly	Lys	Leu	Val	Ile	Asn	Gly	Asn	Pro	Ile	Thr	Ile	Phe	Gln
			85					90						95	
Glu	Arg	Asp	Pro	Ser	Lys	Ile	Lys	Trp	Gly	Asp	Thr	Gly	Ala	Glu	Tyr
			100					105					110		
Val	Val	Glu	Ser	Thr	Gly	Val	Phe	Thr	Met	Glu	Lys	Ala	Gly		
		115				120					125				

```
<210> 102
<211> 1225
<212> DNA
<213> Homo sapien
```

<400> 102									
atggcggcgc	ggtcgctgc	gggggtggcg	gcggcagagg	ggcgggcgcc	cctggcgcca				60
gcggagacgc	cagccgtgac	ggtggcagcg	gcggcgccgg	acctgggctt	gggggaatga				120
gcggcgccgc	gcggggccagc	ggcgagccgc	tgtagccggc	aaagctcccc	tcctcgcttc				180
ccttggcgcc	gcggcgggcg	gcgcgcacg	cgggcgcca	gagcgggctc	ccaccacctc				240
gactcctgcg	accgcgcacg	cacccccacc	cgggcccgcc	ggaatgatga	gctcaagtgc				300
aaccagacc	gcactctacg	cggcgccagc	tacaagaagc	ggcgcgatgc	ctctgtgttc				360
cgacgcgaga	gcgaaggaga	ggtgctactc	tgtagcaatg	ctgcgcctcc	agacagatgg				420
attgtccctg	gaggagcgat	ggagcccgag	gaggagccaa	gtgtggcagc	agttcgatga				480
gtctgtgtag	aggctgtgag	aaagggaca	tgtggaagat	taagtggaa	ttttagaac				540
caggagagag	agcacaggac	gtatgtctat	gtgctcattg	tcactgaagt	gctggaagac				600
tgggaagatt	cagttaacat	tgggaaggag	agggaaatgt	ttaaaataga	agacgccata				660
aaagtgtctc	agtatcaca	accogtcgac	gcacatcat	ttgaaacat	gaggcaaggc				720
tcctcagcca	acaaatgcac	ccagctctgt	gccaccacat	acctcggttc	tgtccagacg				780
tcgatgtcag	catcagatg	actgaagact	tcctctaaga	gaatctgaaa	tgggaacata				840
gactgaagtg	caaatcttcc	ctctcaccc	ggctctctcc	actctcactc	ggctcctct				900
ttcaataaag	cactgtgttc	cagcaaaaga	aggggttat	gataatgttg	cttctgtgtg				960
ttaagtgatg	gggctttttc	ttctgttttt	attgaggggt	gggggtgggt	gtgtaatttg				1020
taagtaattt	tgtgcatgat	ctgtccctcc	ctctctccac	ccctgcagtc	ctctgaagag				1080
agggcaacag	ccttccctcg	ccttggatct	tgaagtgctc	tgtctgtct	tatcctggcc				1140
ctggccagac	gttttctttt	atttttaatt	tttttttttt	attaaaagat	accagatgat				1200
gaataaaaaa	gataaaaaac	tcgaat							1255

<210> 103

<211> 741  
 <212> DNA  
 <213> Homo sapien

<400> 103  
 agaaacctca atcggattca gcaaaggaat ggtgttatta tcaactacata ccaaatgtta 60  
 atcaataact ggcagcaact ttcaagcttt agggggccaag agtttgtgtg ggactatgtc 120  
 atcctcgatg aagcacataa aataaaaacc tcactacta agtcagcaat atgtgctcgt 180  
 gctattctctg caagtaatcg cctcctcctc acaggaaccc caatccagaa taatttaca 240  
 gaactatggt ccctatttga ttttcttgt caagggtccc tgcctgggaac attaaaaact 300  
 tttaagatgg agtatgaaaa tcctattact agagcaagag agaaggatgc taccocagga 360  
 gaaaaagcct tgggatttaa aatatctgaa aacttaattg caatcataaa accctatttt 420  
 ctccaggagga ctaaaagaaga cgtacagaag aaaaagtcaa gcaaccocaga ggccagactt 480  
 aatgaaaaga atccagatgt tgatgccatt tgtgaaatgc ctccctttc caggagaaat 540  
 gattttaatta tttggatcag acttgtgctt ttacaagaag aaatatacag gaaatttgtg 600  
 tcttttagatc atatacaagga gttgctaagt gagacgcgt cacccttggc tgagctagtg 660  
 gtcttaaga agctgtgtga tcactcctagg ctgctgtctg cacgggcttg ttgtttgtga 720  
 aatcttggga cattctctgc t 741

<210> 104  
 <211> 321  
 <212> DNA  
 <213> Homo sapien

<400> 104  
 ttgctctgctg tcatacaaga caccaaaactg ctgtgctata aaagttccaa ggaccagcag 60  
 cctcagatgg aactgccact ccaaggctgt aacattacgt acatcccgaa agacagcaaa 120  
 aagaagaagc acgagctgaa gattactcag cagggcacgg acccgcttgt tctgcgcgtc 180  
 cagagcaagg aacaggccga gcagtggtgt aagtgatca aagaagccta cagtggttgt 240  
 agtggcccg tggattcaga gtgtcctcct ccaccaagct ccccggtgca caaggcagaa 300  
 ctggagaaga aactgtcttc a 321

<210> 105  
 <211> 389  
 <212> DNA  
 <213> Homo sapien

<400> 105  
 cagcactggc cacactataa aattcaggtt cagaaaaaca gggttaagtc cagacagcaa 60  
 cgcttccagc atttattttc ttgacacca tgggcaattt gagaaaattt acccttagaa 120  
 cgaactctgt taaaggtaca gacagtacaa tactttttat tcagaaggtt tctgcataaa 180  
 ggtgatagtc ttttgactta atatatatt ttgtgttctc tttgtttctt ggaatgaagt 240  
 aaggtcatta tttagaagat aatctgggtt gtatttgtgt cgtcagattg aattttcatt 300  
 gcacatgcta cttaattgtc ttaccaataa ataacaaagg gaaagaaac caaatataga 360  
 tgtataataa ggaaaagctg gcctataga 389

<210> 106  
 <211> 446  
 <212> DNA  
 <213> Homo sapien

<400> 106  
 gccacatttg ccctggctcat agtttaaaaca ccaggtcctg tgtcacatct ttttgggtgc 60  
 acaagtatca ctccattgtg cagagagtaa tgtattagtt ctgcccaatt cattcttcac 120  
 ttttatttct tccattttcat tagcatttat atcagctcaa gaagtttaagg tttagaaaatt 180  
 ttccacttca aattttcagt acagaaatgt gctgtgatgt ttgacaagac tatttcatag 240  
 taagttagtt aatgtttatt ggcctctgct ctccctctgt tcagacctag gaagcctgag 300  
 gattacttag ttgtctctgc tctgggtcca caggcagaat ttggcccatc caaagactgg 360



ccaagtgccca	aaaaaaggcc	tgattaggcc	ctgaaattca	gtgaaattct	gcctgaagaa	420
acctcttatt	gaatttgaaa	accata				446

<210> 107  
 <211> 467  
 <212> DNA  
 <213> Homo sapien

<400> 107						
ccgcgcgtgc	cgctgccttc	ctgggattgg	agtctcgagc	ttctctcggt	cgctgcgcgg	60
cggggttcgcg	ccctcttcgcg	gcctcggggc	tgcgagcgctg	gggaaggggt	tggagggggc	120
tgttgatcgc	cgcgtttaag	ttgcgcctcg	ggcgcccatg	tcggccggcg	aggctcgagcg	180
cctagtgtcg	gagctgagcg	gcgggacccg	aggggatgag	gaggaagagt	ggctctatgg	240
cgatgaagat	gaagttgaaa	ggccagaaga	agaaaatgcc	agtgtctaac	ctccatctgg	300
aattgaagat	gaaactgctg	aaaatgggtg	acccaaaccg	aaagtgactg	agaccgaaga	360
tgatagtgat	agtgcacgcg	atgatgatga	agatgatgtg	catgtcacta	taggagacat	420
taaaacggga	gcaccacagt	atggggatga	tggtacagca	cctgtaa		467

<210> 108  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

<400> 108						
gaaagataca	acttcccaca	cccaaaccgc	tttgtggagg	acgacatgga	taagaatgaa	60
atcgctctcg	ttgcgtacccg	ttaccgcagg	tggaagcctg	gagatgatac	tgaccttatt	120
gtccgtttgtg	agcacgatgg	cgtcatgact	ggagccaacg	gggaagtgtc	cttcatcaac	180
atcaagacac	tcaatgagtg	ggattccagg	cactgtaaat	gcgttgactg	gcgtcagaag	240
ctggactctc	agcgaggggc	tgctattgcc	acggagctga	agaacaacag	ctacaagttg	300
gcccggttga	ctcgtctgtg	tttgtggctg	ggatctgagt	acctcaagct	tggttatgtg	360
tctcggatcc	acgtgaaaga	ctcctcacgc	caogtcatcc	taggcaccca	gcagttcaag	420
cctaagtgtg	ttgcgcacca	gatcaacctg	agcgtggaga	atgcctgagg	cattttacgc	480
tgctgcattg	a					491

<210> 109  
 <211> 489  
 <212> DNA  
 <213> Homo sapien

<400> 109						
ctcagatagt	actgaacctc	ttatcaacta	tgttttttca	gtctgacaac	caaggcggct	60
actaagtgc	taaggggcag	gtagtataca	gtgtggataa	gcaggacaaa	ggggtgattc	120
acatcccagg	caggacagag	caggagatca	tgagatttca	tcactcagga	tggtctgtga	180
tttattttat	tttattcttt	tttttttttg	agatggagtc	tcactcttgc	ccaggctgga	240
gtgcagtggt	gcgatcttgg	ctcactgcaa	cctctgcctc	ctgggttcaa	gcagttctcc	300
tgccctcagcc	tcaccaagtag	ctgggattac	agggctccgc	caccatgcc	agccaatttt	360
tgtactttta	gtagagatgg	ggtttcacca	tggtggccag	gctggtctcg	aactcctgac	420
ctcaggtgat	ccactcgctc	cggcctccca	aagtgtcggg	attataggca	tgccgccacca	480
tgcccgggc						489

<210> 110  
 <211> 391  
 <212> DNA  
 <213> Homo sapien

<400> 110						
gcggagtccg	ctggctgacc	cgagcgctgg	tctccgcggg	gaacctctgg	gcattggagag	60
gtctaggtac	ctcggcccg	gagcacgctg	catcgcgagg	ccaggctgcc	gctgtccacg	120

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tggagttcca ggagcaccac ctgagtgagg tgcagaatat ggcattctgag gagaagctgg      180
agcaggtgct gagttccatg aaggagaaca aagtggccat cattggaaaag attcatacc      240
cgatggagta taagggggag ctagcctcct atgatatgcg gctgaggcgt aagttggact      300
tatttgccaa cgtaatccat gtgaagtcac ttcctgggta tatgactcgg cacaacaatc      360
tagacctggt gatctcca gagcagacag a                                     391

```

<210> 111  
 <211> 172  
 <212> PRT  
 <213> Homo sapien

```

<400> 111
Met Met Lys Leu Lys Ser Asn Gln Thr Arg Thr Tyr Asp Gly Asp Gly
 1      5      10
Tyr Lys Lys Arg Ala Ala Cys Leu Cys Phe Arg Ser Glu Ser Glu Glu
 20      25      30
Glu Val Leu Leu Val Ser Ser Ser Arg His Pro Asp Arg Trp Ile Val
 35      40      45
Pro Gly Gly Gly Met Glu Pro Glu Glu Glu Pro Ser Val Ala Ala Val
 50      55      60
Arg Glu Val Cys Glu Glu Ala Gly Val Lys Gly Thr Leu Gly Arg Leu
 65      70      75      80
Val Gly Ile Phe Glu Asn Gln Glu Arg Lys His Arg Thr Tyr Val Tyr
 85      90      95
Val Leu Ile Val Thr Glu Val Leu Glu Asp Trp Glu Asp Ser Val Asn
100      105      110
Ile Gly Arg Lys Arg Glu Trp Phe Lys Ile Glu Asp Ala Ile Lys Val
115      120      125
Leu Gln Tyr His Lys Pro Val Gln Ala Ser Tyr Phe Glu Thr Leu Arg
130      135      140
Gln Gly Tyr Ser Ala Asn Asn Gly Thr Pro Val Val Ala Thr Thr Tyr
145      150      155      160
Ser Val Ser Ala Gln Ser Ser Met Ser Gly Ile Arg
165      170

```

<210> 112  
 <211> 247  
 <212> PRT  
 <213> Homo sapien

```

<400> 112
Arg Asn Leu Asn Arg Ile Gln Gln Arg Asn Gly Val Ile Ile Thr Thr
 1      5      10      15
Tyr Gln Met Leu Ile Asn Asn Trp Gln Gln Leu Ser Ser Phe Arg Gly
 20      25      30
Gln Glu Phe Val Trp Asp Tyr Val Ile Leu Asp Glu Ala His Lys Ile
 35      40      45
Lys Thr Ser Ser Thr Lys Ser Ala Ile Cys Ala Arg Ala Ile Pro Ala
 50      55      60
Ser Asn Arg Leu Leu Leu Thr Gly Thr Pro Ile Gln Asn Asn Leu Gln
 65      70      75      80
Glu Leu Trp Ser Leu Phe Asp Phe Ala Cys Gln Gly Ser Leu Leu Gly
 85      90      95
Thr Leu Lys Thr Phe Lys Met Glu Tyr Glu Asn Pro Ile Thr Arg Ala
100      105      110
Arg Glu Lys Asp Ala Thr Pro Gly Glu Lys Ala Leu Gly Phe Lys Ile
115      120      125
Ser Glu Asn Leu Met Ala Ile Ile Lys Pro Tyr Phe Leu Arg Arg Thr

```

130		135		140
Lys Glu Asp Val Gln	Lys Lys Ser Ser	Asn Pro Glu Ala Arg	Leu	
145	150	155	160	
Asn Glu Lys Asn Pro	Asp Val Asp Ala Ile Cys	Glu Met Pro Ser	Leu	
	165	170	175	
Ser Arg Arg Asn Asp	Leu Ile Ile Trp Ile Arg	Leu Val Pro Leu	Gln	
	180	185	190	
Glu Glu Ile Tyr Arg	Lys Phe Val Ser Leu Asp	His Ile Lys Glu	Leu	
	195	200	205	
Leu Met Glu Thr Arg	Ser Pro Leu Ala Glu Leu Gly	Val Leu Lys Lys		
	210	215	220	
Leu Cys Asp His Pro	Arg Leu Leu Ser Ala Arg	Ala Cys Cys Leu	Leu	
225	230	235	240	
Asn Leu Gly Thr Phe	Ser Ala			
	245			

<210> 113  
 <211> 107  
 <212> PRT  
 <213> Homo sapien

<400> 113
Leu Leu Cys Val Ile Lys Asp Thr Lys Leu Leu Cys Tyr Lys Ser Ser
1 5 10 15
Lys Asp Gln Gln Pro Gln Met Glu Leu Pro Leu Gln Gly Cys Asn Ile
20 25 30
Thr Tyr Ile Pro Lys Asp Ser Lys Lys Lys His Glu Leu Lys Ile
35 40 45
Thr Gln Gln Gly Thr Asp Pro Leu Val Leu Ala Val Gln Ser Lys Glu
50 55 60
Gln Ala Glu Gln Trp Leu Lys Val Ile Lys Glu Ala Tyr Ser Gly Cys
65 70 75 80
Ser Gly Pro Val Asp Ser Glu Cys Pro Pro Pro Ser Ser Pro Val
85 90 95
His Lys Ala Glu Leu Glu Lys Lys Leu Ser Ser
100 105

<210> 114  
 <211> 155  
 <212> PRT  
 <213> Homo sapien

<400> 114
Glu Arg Tyr Asn Phe Pro Asn Pro Asn Pro Phe Val Glu Asp Asp Met
1 5 10 15
Asp Lys Asn Glu Ile Ala Ser Val Ala Tyr Arg Tyr Arg Arg Trp Lys
20 25 30
Leu Gly Asp Asp Ile Asp Leu Ile Val Arg Cys Glu His Asp Gly Val
35 40 45
Met Thr Gly Ala Asn Gly Glu Val Ser Phe Ile Asn Ile Lys Thr Leu
50 55 60
Asn Glu Trp Asp Ser Arg His Cys Asn Gly Val Asp Trp Arg Gln Lys
65 70 75 80
Leu Asp Ser Gln Arg Gly Ala Val Ile Ala Thr Glu Leu Lys Asn Asn
85 90 95
Ser Tyr Lys Leu Ala Arg Trp Thr Cys Cys Ala Leu Leu Ala Gly Ser
100 105 110
Glu Tyr Leu Lys Leu Gly Tyr Val Ser Arg Tyr His Val Lys Asp Ser

115	120	125
Ser Arg His Val Ile Leu Gly Thr Gln Gln Phe Lys Pro Asn Glu Phe		
130	135	140
Ala Ser Gln Ile Asn Leu Ser Val Glu Asn Ala		
145	150	155

<210> 115  
 <211> 129  
 <212> PRT  
 <213> Homo sapien

<400> 115
Gly Val Arg Trp Leu Thr Arg Ala Leu Val Ser Ala Gly Asn Pro Gly
1 5 10 15
Ala Trp Arg Gly Leu Ser Thr Ser Ala Ala His Ala Ser Arg
20 25 30
Ser Gln Ala Ala Val Pro Val Glu Phe Gln Glu His His Leu Ser
35 40 45
Glu Val Gln Asn Met Ala Ser Glu Glu Lys Leu Glu Gln Val Leu Ser
50 55 60
Ser Met Lys Glu Asn Lys Val Ala Ile Ile Gly Lys Ile His Thr Pro
65 70 75 80
Met Glu Tyr Lys Gly Glu Leu Ala Ser Tyr Asp Met Arg Leu Arg Arg
85 90 95
Lys Leu Asp Leu Phe Ala Asn Val Ile His Val Lys Ser Leu Pro Gly
100 105 110
Tyr Met Thr Arg His Asn Asn Leu Asp Leu Val Ile Ile Arg Glu Gln
115 120 125
Thr

<210> 116  
 <211> 550  
 <212> DNA  
 <213> Homo sapien

<400> 116	
gaattcgcca ccagcctcag agccccccag cccggctacc accccctgcg gaaaggtacc	60
catctgcatt cctgcccgtc gggacactggt ggacagtcca gctcctctgg cctctagcct	120
tggtctaacg ctgcctagag ccaaggagct catcctgaat gaccttcccg ccagcactcc	180
tgcttccaaa tctgtgact cctcccgcgc ccaggacgct tccaccccca ggcccagctc	240
ggccagtcac ctctgccagc ttgctgccaa gccagcacct tccacggaca gcgtgcacct	300
gaggagcccc ctgactctgt ccagtccctt caccacgtcc ttacagcctgg gctccacag	360
cactctcaac ggagacctct ccgtgccag ctctctacgtc agcctccacc tgtcccccca	420
ggtcagcagc tctgtggtgt acggacgtc ccccgatgat gcatttgagt ctcatcccca	480
tctccgaggg tcatccgtct ctctctccct acccagcacc cctgggggaa agccgcgccta	540
ctccttcac	550

<210> 117  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 117	
ttctgagggg aagccgagtg gtagtgggcca cccggcgggc gtgacaatga gttttcttgg	60
aggctttttt ggtccattt gtgagattga tgttgccctt aatgatgggg aaaccaggaa	120
aatggcagaa atgaaaactg aggatggcaa agta	154

<210> 118  
 <211> 449  
 <212> DNA  
 <213> Homo sapien

<400> 118  
 gaattcggca ccagggccgc gaggccgagt gtgcgcgcca tggcttcgcc gcagctctgc 60  
 cgcgcgctgg tgtcggcgca atgggtggcg gaggcgctgc gggcccgcg cgctgggcag 120  
 cctctgcagc tgcctggcgc ctctgtgtac ctgcgcgaagc tggggcgcgca cgcgcgacgc 180  
 gagttcgagg agcgccacat ccggggcgcc gctttcttcg acatcgacca gtgcagcgac 240  
 gcacacctgc cctacgacca catgctgccc ggggcccagc atttcgcgga gtacgcaggc 300  
 cgctcgggcg tggggcgccg caccacgctc gtgatctacg acgccagcgc ccagggccctc 360  
 tactcgcgcc cgcgcgtctg gtggatgttc cgcgccttcg gccaccaagc cgtgtcactg 420  
 ctgtatggcg gctccgcca ctggctgcg 449

<210> 119  
 <211> 642  
 <212> DNA  
 <213> Homo sapien

<400> 119  
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 ctgtccaaac cttctctctc cctgtcaaca gtggccagcc ccccaactat gagatgctca 120  
 aggaggagca cgaggtggct gtgctggggg cgccccacaa cctctgtccc ccgacgtcca 180  
 cgtgtatcca catccgcagc gagacctccg tgcgcgacca tgtcgtctgg tccctgttca 240  
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 ctagggacag gaagatggtt ggcgacgtga cggggcgcca ggccatgccc tccaccgcca 360  
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 tccagtgct gatctccag gctatggat agatcaggag gcatcactga ggccaggagc 480  
 tctgccaatg aactgtatcc cactgaactc aacttccatt cctcgccctg ccccgaggc 540  
 cgagtcctgt atcagccctt tatcctcaca cgcttttcta caatggcatt caataaagt 600  
 cacgtgttct tggtagaaaa aaaaaaaaaa aaaaaactcg ag 642

<210> 120  
 <211> 603  
 <212> DNA  
 <213> Homo sapien

<400> 120  
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 catgtccacc atgtccacaa tccacacctc ctctactcca gagaccacc acacctccac 180  
 agtgctgacc accacagcca ccatgacaag ggccaccaat tccacggcca caccctctc 240  
 cactctgggg acgaccggga tctctactga gctgaccaca acagccaata caactgagc 300  
 cactggatcc acggccaccc tgtctccac ccaggggacc acctggatcc tccacgagcc 360  
 gagcactata gccacgtga tgggtgccac cgggtccag gccacgcct cctccactct 420  
 gggaacagct cacaccccca aagtggtgac caccatggcc actatgcca cagccactgc 480  
 ctccacggtt cccagctcgt ccaccgtggg gaccaccgc accctgcag tgcctcccag 540  
 cagcctgcca acctcagcg tgtccactgt gtctctcca gtctcaca cctcgagacc 600  
 cac 603

<210> 121  
 <211> 178  
 <212> PRT  
 <213> Homo sapien

<400> 121  
 Ser Glu Pro Pro Ser Pro Ala Thr Thr Pro Cys Gly Lys Val Pro Ile

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      1           5           10           15
Cys Ile Pro Ala Arg Arg Asp Leu Val Asp Ser Pro Ala Ser Leu Ala
      20           25           30
Ser Ser Leu Gly Ser Pro Leu Pro Arg Ala Lys Glu Leu Ile Leu Asn
      35           40           45
Asp Leu Pro Ala Ser Thr Pro Ala Ser Lys Ser Cys Asp Ser Ser Pro
      50           55           60
Pro Gln Asp Ala Ser Thr Pro Arg Pro Ser Ser Ala Ser His Leu Cys
      65           70           75           80
Gln Leu Ala Ala Lys Pro Ala Pro Ser Thr Asp Ser Val Ala Leu Arg
      85           90           95
Ser Pro Leu Thr Leu Ser Ser Pro Phe Thr Thr Ser Phe Ser Leu Gly
      100           105           110
Ser His Ser Thr Leu Asn Gly Asp Leu Ser Val Pro Ser Ser Tyr Val
      115           120           125
Ser Leu His Leu Ser Pro Gln Val Ser Ser Ser Val Val Tyr Gly Arg
      130           135           140
Ser Pro Val Met Ala Phe Glu Ser His Pro His Leu Arg Gly Ser Ser
      145           150           155           160
Val Ser Ser Ser Leu Pro Ser Ile Pro Gly Lys Lys Pro Ala Tyr Ser
      165           170           175
Phe His

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<210> 122
<211> 36
<212> PRT
<213> Homo sapien

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<400> 122
Met Ser Phe Leu Gly Gly Phe Phe Gly Pro Ile Cys Glu Ile Asp Val
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Ala Leu Asn Asp Gly Glu Thr Arg Lys Met Ala Glu Met Lys Thr Glu
      20           25           30
Asp Gly Lys Val
      35

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<210> 123
<211> 136
<212> PRT
<213> Homo sapien

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<400> 123
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Ala Glu Ala Leu Arg Ala Pro Arg Ala Gly Gln Pro Leu Gln Leu Leu
      20           25           30
Asp Ala Ser Trp Tyr Leu Pro Lys Leu Gly Arg Asp Ala Arg Arg Glu
      35           40           45
Phe Glu Glu Arg His Ile Pro Gly Ala Ala Phe Phe Asp Ile Asp Gln
      50           55           60
Cys Ser Asp Arg Thr Ser Pro Tyr Asp His Met Leu Pro Gly Ala Glu
      65           70           75           80
His Phe Ala Glu Tyr Ala Gly Arg Leu Gly Val Gly Ala Ala Thr His
      85           90           95
Val Val Ile Tyr Asp Ala Ser Asp Gln Gly Leu Tyr Ser Ala Pro Arg
      100           105           110
Val Trp Trp Met Phe Arg Ala Phe Gly His His Ala Val Ser Leu Leu

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115 120 125  
 Asp Gly Gly Leu Arg His Trp Leu  
 130 135

<210> 124  
 <211> 133  
 <212> PRT  
 <213> Homo sapien

<400> 124  
 Met Asn His Thr Val Gln Thr Phe Phe Ser Pro Val Asn Ser Gly Gln  
 1 5 10 15  
 Pro Pro Asn Tyr Glu Met Leu Lys Glu Glu His Glu Val Ala Val Leu  
 20 25 30  
 Gly Ala Pro His Asn Pro Ala Pro Thr Ser Thr Val Ile His Ile  
 35 40 45  
 Arg Ser Glu Thr Ser Val Pro Asp His Val Val Trp Ser Leu Phe Asn  
 50 55 60  
 Thr Leu Phe Met Asn Pro Cys Cys Leu Gly Phe Ile Ala Phe Ala Tyr  
 65 70 75 80  
 Ser Val Lys Ser Arg Asp Arg Lys Met Val Gly Asp Val Thr Gly Ala  
 85 90 95  
 Gln Ala Tyr Ala Ser Thr Ala Lys Cys Leu Asn Ile Trp Ala Leu Ile  
 100 105 110  
 Leu Gly Ile Leu Met Thr Ile Leu Leu Ile Val Ile Pro Val Leu Ile  
 115 120 125  
 Phe Gln Ala Tyr Gly  
 130

<210> 125  
 <211> 195  
 <212> PRT  
 <213> Homo sapien

<400> 125  
 Thr Thr Ala Thr Thr Thr Ala Ser Thr Gly Ser Thr Ala Thr Pro Ser  
 1 5 10 15  
 Ser Thr Pro Gly Thr Ala Pro Pro Pro Lys Val Leu Thr Ser Pro Ala  
 20 25 30  
 Thr Thr Pro Met Ser Thr Met Ser Thr Ile His Thr Ser Ser Thr Pro  
 35 40 45  
 Glu Thr Thr His Thr Ser Thr Val Leu Thr Thr Thr Ala Thr Met Thr  
 50 55 60  
 Arg Ala Thr Asn Ser Thr Ala Thr Pro Ser Ser Thr Leu Gly Thr Thr  
 65 70 75 80  
 Arg Ile Leu Thr Glu Leu Thr Thr Thr Ala Thr Thr Thr Ala Thr  
 85 90 95  
 Gly Ser Thr Ala Thr Leu Ser Ser Thr Pro Gly Thr Thr Trp Ile Leu  
 100 105 110  
 Thr Glu Pro Ser Thr Ile Ala Thr Val Met Val Pro Thr Gly Ser Thr  
 115 120 125  
 Ala Thr Ala Ser Ser Thr Leu Gly Thr Ala His Thr Pro Lys Val Val  
 130 135 140  
 Thr Thr Met Ala Thr Met Pro Thr Ala Thr Ala Ser Thr Val Pro Ser  
 145 150 155 160  
 Ser Ser Thr Val Gly Thr Thr Arg Thr Pro Ala Val Leu Pro Ser Ser  
 165 170 175  
 Leu Pro Thr Phe Ser Val Ser Thr Val Ser Ser Ser Val Leu Thr Thr

Leu Arg Pro	180	185	190
195			
<210> 126			
<211> 509			
<212> DNA			
<213> Homo sapien			
<400> 126			
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actgcagcct gggagctcta ttccacctta caacaccgag gtgactgaga ccaccattgt	180		
gatcacatgg acgcctgctc caagaattgg ttttaagctg ggtgtacgac caagccaggg	240		
aggagaggca ccacgagaag tgacttcaga ctacggaagc atcgtttgtg ccggcttgac	300		
tcacaggatga gaatacgtct acaccatoca agtcctgaga gatggacagg aaagagatgc	360		
gccaatgtga aacaaagtgg tgacaccatt gtctccacca acaaaacttg atctggaggc	420		
aaacccctgac actggagtgc tcacagcttc ctggagaggga gcaccacccc agacattact	480		
gggtatagaa ttaccacaac cccatacaaa	509		
<210> 127			
<211> 500			
<212> DNA			
<213> Homo sapien			
<400> 127			
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cgcccccggg gccggtcccg gagggctcga tccgcattcta cagcatgagg ttctggccgt	120		
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tcaacctgaa aaataagcct gagtgtttct ttaagaaaaa tccctttgtt ctggtgccag	240		
ttctggaaaa cagtccagggt cagctgatct acgagtctgc catcacctgt gagtacctgg	300		
atgaagcata cccagggaag aagctgtttg cggatgacct ctatgagaaa gcttgccaga	360		
agatgatctt agagtgtttt tctaaggtgc catccttggg aggaagcttt attagaagcc	420		
aaaataaaga agactatgct tgcctaaaaa aagaatttcg taaagaattt accaagctag	480		
aggaggttct gactaataag	500		
<210> 128			
<211> 500			
<212> DNA			
<213> Homo sapien			
<400> 128			
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tgaatgcaga agcttctgtg ccaaaagatg tgggaattgt tgcccttgag atctattttc	180		
cttctcaata tgttgatcaa gcagagtttg aaaaatatga ttggttagat gctggaaagt	240		
ataccattlg ctgtggccag gccaaagatg gcttctgcac agatagagaa gatattaaat	300		
ctctttgcat gactgtgggt cagaatctta tggagagaaa taacctttcc tatgattgca	360		
ttgggcccgt ggaagttgga acagagacaa tcatcgacaa atcaaaagtct gtgaagacta	420		
atttgatgca gctgtttgaa gagtctggga atacagatat agaaggaatc gacacaacta	480		
atgcattgcta tggaggcaca	500		
<210> 129			
<211> 497			
<212> DNA			
<213> Homo sapien			
<400> 129			



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taaggaaaaa	ctcattgcac	cagttgcgga	agaagaggca	acagttccaa	acaataagat	120
cactgtagtg	ggtgttgga	aagttggtat	ggcgtgtgct	atcagcattc	tgggaaagtc	180
ctctgctagt	gaacttgctc	ttgtggtatg	tttggaagat	aagcttaaag	gagaaatgat	240
ggatctcgag	catgggagct	tattcttcca	gacacctaaa	attgtggcag	ataaagatta	300
ttctgtgacc	gccaaattcta	agattgtagt	ggtaaactgca	ggagtccgtc	agcaagaagg	360
ggagagtcgg	ctcaatctgg	tgcagagaaa	tgtaaatgtc	ttcaaatcca	ttattcctca	420
gatcgtaag	tacagtctct	attgcatcat	aattgtgggt	tccaaaccag	tggacattct	480
tacgtatggt	acctgga					497

<210> 130  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<400> 130	
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gcgcgtgtcg	ccaccatggc
60	
tccgcaccgc	cccgcgccgc
cgctgctttg	cgcgcgtgtc
120	
gctgcgccgc	cgcgcgccca
ctgcgtcgcg	ggggcgctgc
180	
cggggtcccc	gagcgcgccg
ccaacacgcat	ggtgtgtgaa
240	
agggaaaggag	ctgtgcctgc
agatctggcg	tggtggagaaa
300	
cccaccaacc	tttatggaga
ctcttccacg	ggcgacgcct
360	
cagcttaaga	acggaaaatc
ttg	
480	
383	

<210> 131  
 <211> 509  
 <212> DNA  
 <213> Homo sapien

<400> 131	
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ccgcattctc	ttttgcgtcg
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agacaccatg	gggaaggtga
aggtcggagt	caacggattt
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caccagggtc	gcttttaact
ctggtaaagt	ggatattgtt
180	
tgacctcaac	tacatggttt
acatgttcca	atatgattcc
240	
caccgtcaag	gctgagaacg
ggaagcttgt	catcaatgga
300	
ggagcgagat	ccctccaaaa
tcaagtgggg	cgatgctggc
360	
cactggccgt	cttccaccac
atggagaagg	ctggggctca
420	
gggtcatcat	ctctgccccc
tctgctgacg	cccccatgtt
480	
agaagtatga	caacagcctc
aagatcatc	
509	

<210> 132  
 <211> 357  
 <212> DNA  
 <213> Homo sapien

<400> 132	
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gaagccccta	gaccacagct
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ggagagatcct	cttcttgtgt
cgacgagcaa	caggtgcccc
120	
aatctgggtc	tgagttgaag
aagcctgggg	cctcagtgaa
180	
gacacatctt	cagtatctat
ggtttgtaatt	gggtgcgaca
240	
agtggatggg	atggatcaaa
gtcgacactg	cgaacccaac
300	
gacgatttgt	cttctccctg
gacacctctg	tcagcaccgc
360	
	atatctgcag
	atcagca
420	

<210> 133  
 <211> 468  
 <212> DNA  
 <213> Homo sapien

<400> 133  
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ccgagacctg gcccggtctc cactccatga cgcattttcg caccgccatg tcccgcccg 120  
gccgcgggga gccccgcttc atctcagtggt gctacgtgga cgacacgcag tctcgtgaggt 180  
tcgacagcga cgcgcgcgagt ccgagagagg agccgcgggc gccgtggata gacgaggagg 240  
ggccggagta ttgggacccg aacacacaga tcttcaagac caacacacag actgacccag 300  
agagcctgcg gaacctgcgc ggctactaca accagagcga ggccgggtct cacacctcc 360  
agagcatgta cggctgcgac gtggggcccg acgggcgcct cctccgcggg cataaccagt 420  
acgctacga cggcaaggat tacatcgccc tgaacgagga cctgcgct 468

<210> 134  
<211> 214  
<212> DNA  
<213> Homo sapien

<400> 134  
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agtgcctggt tctctgtctc caccaggaa cccagcccat gtctcgccag tcaagtgtgt 120  
ccttcgggag cggggcgagt cgtagcttca gcaccgcctc tgccatcacc ccgtctgtct 180  
ccgcaccag cttcacctcc gtgtccggt ccgg 214

<210> 135  
<211> 355  
<212> DNA  
<213> Homo sapien

<400> 135  
gaattcggca cgaggtgaac aggaccgctc gccatgggcc gtgtgatccg tggacagagg 60  
aaggcgcccg ggtctgtggt ccgcgcgcac gtgaagcacc gtaaggcgcc tgcgcgcctg 120  
cgcgcgtggt atttcgtgta cgcgcacggc tacatcaagg gcacgtctca ggacatcctc 180  
cacgaccgag gccgcgcgc gccctcgcgc aaggtgtctc tccgggatcc gtatcgggtt 240  
aagaacggga cggagctggt cattgcgcgc gagggcattc acacgggcca gtttgtgat 300  
tcgggcaaga aggccagct caacattgac aatgtgtccc ctgtgggcac catgc 355

<210> 136  
<211> 242  
<212> DNA  
<213> Homo sapien

<400> 136  
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gcccgattg cagacggagt ctcttcaact cagtgtcaa tggcgccag gctggagtg 120  
agtgtgtgta tctcggctcg ctacaacatc cactctccag cagcctgcct tggcctccca 180  
aagtcgagcag attgcagctc tctgcccgcc cgcaccacct gtctgggaag tgaggatgct 240  
gt 242

<210> 137  
<211> 424  
<212> DNA  
<213> Homo sapien

<400> 137  
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gccaggagca agccgagagc cagccggccg gcgcactccg actccgagca gtctctgtcc 120  
ttcgaccaga gccccgcgcg ctctccggga cccctgcccc cggggcagcg ctgccaaact 180  
gcggccatc gagacccggt cccagcgggc cgcacccgcg agcggggcgcc aggcacagct 240  
cactccgctg tcgcaccacc gctgcacccg cgtgcaggag aaggaggacc tgcaaggagt 300  
caatgatcgc ttggcggtct acatcgaccg tgtgcgtcgc ctggaaacgg agaagcagag 360

gctgcgcctt cgcataccgc agtctgaaga ggtgggtcagc cgcgaggtgt ccggcatcaa 420  
ggcc 424

<210> 138  
<211> 448  
<212> DNA  
<213> Homo sapien

<400> 138  
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agacttaacct gtccactca cagatttgaa gattcaatat actaagatct tcatatacaa 120  
tgaatggcat gattcagtg gtggcaagaa atttcctgtc tttaatcctg caactgagga 180  
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actattatac aagttggctg atttaacga aagagatcgt ctgctgctgg ccgacaatgg 360  
agtcaatgaa tgggtgaaaa ctctattcca atgcatactt gaatgattta gcaggctgca 420  
tcaaaacatt gcgctactgt gcaggttg 448

<210> 139  
<211> 510  
<212> DNA  
<213> Homo sapien

<400> 139  
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ccccaggag ctgcgcaagt gctgcgagga cggcatgcgg gagaacccca tgaggttctc 120  
gtgcagcgc cggaccggtt tcatctccct ggcgaggcgt gcaagaaggt ctctctggac 180  
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gagcatgtgc gacaagaaag ggaatctgtg ggcagacccc ttcgaggtca cagtaatgca 480  
ggacttcttc atcgacctgc ggcatacccta 510

<210> 140  
<211> 360  
<212> DNA  
<213> Homo sapien

<400> 140  
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cgatgttttg ggggtcaaac ccaatgctac tcaggaagaa ttgaaaaagg cttatagtaa 180  
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ttctcaagct tacgaagttc tctctgatgc aagaaaaagg gaattatatg acaaggagg 300  
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<210> 141  
<211> 483  
<212> DNA  
<213> Homo sapien

<400> 141  
gaattcggca cgagagcaga ggctgatctt tgcggaaaa cagctggaag atgggctgca 60  
ccctgtctga ctacaacatc cagaaagagt ccaccctgca cctgggtgctc cgtctcagag 120  
gtgggatgca aatcttctgtg aagacactca ctggcaagac catcacctt gaggtggagc 180  
ccagtgacac catcgagaac gtcaaagcaa agatccagga caagggaagg attcctcctg 240  
accagcagag gttgatcttt gccggaaagc agctggaaga tgggcgcacc ctgcttgact 300

aacaacatcca	gaaagagtct	accctgcacc	tgggtgctccg	tctcagaggt	gggagtcaga	360
tcttcgtgaa	gacctgact	ggtaaagcca	tcaccctcga	ggtggagccc	agtgcaccca	420
tcgagaatgt	caaggcaag	atccaagata	aggaagcatt	tcctcctgat	cagcagaggt	480
tga						483

<210> 142  
 <211> 500  
 <212> DNA  
 <213> Homo sapien

<400> 142						
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gaatcacccc	atgttgggtg	agctgaaaaa	tggggagacg	tacaatggac	acctggtgag	180
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aggcctgcag	cagcagaagc	agcagaagag	ccgcggcgatg	ggcgccgctg	ggcgaggtgt	420
gtttggtggc	cgggcccgag	gtgggatccc	gggcacaggc	agaagccagc	cagagaagaa	480
gcctggcaga	caggcgggca					500

<210> 143  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<400> 143						
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ctcagaagaa	agcgatcgcc	cccgaggcag	gaagggcggc	tccggtgcag	ggcgcccgcc	120
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gcctgaagga	cccatggaca	cgtgactcca	gtgtttctca	caacatctta	gatcaagttg	360
gtttgcacaa	catttgcctc	tacttgggac	aaagcaagaa			400

<210> 144  
 <211> 243  
 <212> DNA  
 <213> Homo sapien

<400> 144						
gaattcggca	cgagccagct	cctaaccgcg	agtgatccgc	cagcctccgc	ctcccagggt	60
gcccgagattg	cagacggagt	ctccttcaact	cagtgctcaa	tgggtgccag	gctggaggtgc	120
agtggtgtga	tctcggtctg	ctacaacatc	cacctccagc	cagcctgcct	tggcctccca	180
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ctg						243

<210> 145  
 <211> 450  
 <212> DNA  
 <213> Homo sapien

<400> 145						
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cggcgccggc	ggcggtgggt	gttacaaccg	cagcagtggt	ggctatgaac	ccagagggtcg	120
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<210> 146  
 <211> 451  
 <212> DNA  
 <213> Homo sapien

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gcggcagcgc	aggctgacaa	gcccaacagc	aagcgctcac	ggcggcagcg	caacaacgag	420
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<210> 147  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<400> 147						
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<210> 148  
 <211> 503  
 <212> DNA  
 <213> Homo sapien

<400> 148						
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<210> 149  
 <211> 1061  
 <212> DNA  
 <213> Homo sapien

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&lt;210&gt; 150

&lt;211&gt; 781

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 150

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&lt;210&gt; 151

&lt;211&gt; 3275

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 151

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&lt;210&gt; 152

&lt;211&gt; 2179

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 152

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<210> 153  
 <211> 2109  
 <212> DNA  
 <213> Homo sapien

<400> 153						
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&lt;210&gt; 154

&lt;211&gt; 1411

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 154

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&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 155

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<212> DNA  
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<212> DNA  
<213> Homo sapien

<400> 158

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&lt;210&gt; 159

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 159

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&lt;210&gt; 160

&lt;211&gt; 848

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 160

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ggttctcgaa	aaaaaaaac	taaaaaaac	tcgag			395

<210> 165  
 <211> 503  
 <212> DNA  
 <213> Homo sapien

<400> 165

gaattcggca	ccagggaacgc	tccgtgagag	gcggaggagc	ggtaactacc	ccggttgccg	60
acagctcggc	gctccttccc	gctccctcac	acacccggcc	cagcccgac	ccgcagtaga	120
agatggtgaa	agaaaacaat	tactacgatg	ttttgggggt	caaaccgaat	gctactcagg	180
aagaattgaa	aaaggtttat	aggaactctg	ccttgaaagta	ccatcctgat	aagaacccaa	240
atgaaggaga	gaagttttaa	cagatttctc	aagctttacga	agttctctct	gatgcagaata	300
aaagggaatt	atatgacaaa	ggaggagaa	aggcaattaa	agaggggtgga	gcaggtggcg	360
gttttggctc	ccccatggac	atctttgata	tgttttttgg	aggaggagga	aggatgcaga	420
ggaaaaggag	aggtaaaaat	gtgttacatc	agctctcagt	aacccataga	gacttatata	480
atggtgcac	aagaaaactg	gct				503

<210> 166  
 <211> 893  
 <212> DNA  
 <213> Homo sapien

<400> 166

gaattcggca	cgagaggaac	ttctcttgac	gagaagagag	accaaggagg	ccaagcaggg	60
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actacatctc	aaaaaaaaaa	aaaaaaaaaa	aaaagaaaga	aaagaaagaa	aaaaagaaag	180
aacggaagta	gttgtaggta	gggtatggt	ggatgagtc	tggtttctgt	tacttataac	240
aacaacaaca	acaaaaaacg	ctgaaactgg	gtaatttata	aagaaaagga	aaaaaagcag	300
aaaaaaaaat	ggaagaagag	aaaggaaaag	aagacaaata	aatgaaattt	atgtattaca	360
gtttctgaag	ctgagacatc	ccagggtcaag	gggtccacact	tggcgagggc	tttcttgctg	420
gtgggactc	tttgtggagt	cctgggacag	tgacagaagga	tcacgcctcc	ctaccgcctc	480
aagcccaagc	ctcagccatg	gcacgcccc	tggtatcagg	cattggcctc	ctcgtggcca	540
ctctccacaa	gtactccggc	aggagggtg	acaagcacac	cctgagcaag	aaggagctga	600
aggagctgat	ccagaaggag	ctcaccattg	gctcgaaagt	gcaggatgct	gaaattgcaa	660
ggctgatgga	agacttggac	cggaacaagg	accaggagggt	gaacttccag	gagtatgtca	720
ccttctctgg	ggccttggct	ttgatctaca	atgaagccct	caagggcctga	aaataaatag	780
ggaagatgga	gacaccctct	gggggtcctc	tctgagtc	aatccagtgt	gggtaatgtg	840
acaataaatt	ttttttggct	aaattttaa	aaaaaaaaa	aaaaaaactg	gag	893

<210> 167  
 <211> 549  
 <212> DNA  
 <213> Homo sapien

<400> 167

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ttcgaccgca	gcgcccgccg	ctttccggga	ccccctcccc	gcggggcagc	ctgcccaact	180
gdcggccatg	gagaccccg	ccacagcgcc	cgccaccgcc	agcggggcgc	agggcagctc	240
cactccgctg	tcgcccaccc	gcacacccg	gctgcaggag	aaggaggacc	tcgacagctc	300
caatgatcgc	ttggcggtct	acatcgaccg	tgtgcgctcg	ctggaaaacg	agaaacgagc	360
gctgcgcctt	cgcatcaccc	agctctgaaga	gggtggtcagc	cgcgagggtg	ccggcatcaa	420
ggccgcctac	gaggccgagc	tgggggatgc	ccgcaagacc	cttgactcag	tagccagaga	480

gcgcgccccg	ctgcagctgg	agctgagcaa	agtgccgtgaa	gagtttaagg	agctgaaagc	540
gcgcaatac						549

<210> 168  
 <211> 547  
 <212> DNA  
 <213> Homo sapien

<400> 168						
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tcaaaatgga	ggaagagagc	ggcgcgcccg	gcgtgcccgag	cgccaacggg	gctccggggc	120
ctaagggtga	aggagaacga	cctgctcaga	atgagaagag	gaaggagaaa	aacataaaaa	180
gaggaggcaa	tcgctttgag	ccatatgccca	atccaaactaa	aagatacaga	gccttcatta	240
caaacatacc	ttttgatgtg	aaatggcagc	cacttaaaaga	cctgggtaaa	gaaaaagttg	300
gtgaggtaac	atcacgtggg	ctcttaattg	acgctgaagg	aaagtcaagg	ggatgtgctg	360
ttgttgtaatt	caagatggaa	gagagcatga	aaaaagctgc	ggaagtccta	aacaagcata	420
gtctagcggg	aagaccactg	aaagtcacaa	aagatcctga	tggtgaaacat	gccaggagag	480
caatgcaaaa	ggctggaaga	cttggaagca	cagtatttgt	agcaaatctg	gattataaag	540
ttggctg						547

<210> 169  
 <211> 547  
 <212> DNA  
 <213> Homo sapien

<400> 169						
gaattcggca	ccaggagctc	gactgtgctc	gctgctcagc	gccgcaccgg	gaagatgagg	60
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aaaactgtga	gatgggtgct	agtgtoggag	catgaggcca	ctaagtgcga	gagtttccgc	180
gaccatgaa	aaagcgtcat	tccatccgat	ggctccagtg	ttgcttgtgt	gaagaagacc	240
tcctaccttg	attgcatcag	ggccattgct	gcaaacgaag	cgagtcctgt	gacactggat	300
gcaggtttgg	tgtatgatgc	ttacctggct	cccaataacc	tgaagcctgt	ggtggcagag	360
ttctatgggt	caaaagagga	tcacagagct	ttctattatg	ctgttgctgt	ggtgaagaag	420
gatagtggct	tcagatgaa	ccagcttcga	ggcaagaagt	cctgccacac	gggtctaggc	480
aggtccgctg	ggtggaacat	cccataggc	ttactttact	gtgacttacc	tgagccacgt	540
aaacctc						547

<210> 170  
 <211> 838  
 <212> DNA  
 <213> Homo sapien

<400> 170						
gaattcggca	ccagaggagc	tggcctgctg	ctgcgccacg	atgtccgggg	agtccagcag	60
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cagcatgagg	ttctgcccg	ttgctgagag	gacgcgtcta	gtcctgaagg	ccaagggaat	180
caggcatgaa	gtcatcaata	tcaacctgaa	aaataagcct	gagtggtctc	ttaaagaaaa	240
tcctcttgg	ctgggtccag	ttctggaaaa	cagtcagggt	cagctgatct	acagagtctgc	300
catcacctcg	gagtcactgg	atgaagcata	cccagggaag	aagctgttgc	cgatgaccc	360
ctatgagaaa	gcttgccaga	agatgatctt	agagttgttt	tctaaaggtc	catccttggt	420
aggaagcttt	attagaagcc	aaaataaaga	agactatgat	ggcctaaaa	aagaatttccg	480
taaaagattt	accaagctag	aggaggttct	gactaataag	aagacgacct	tcctttgggtg	540
caattctatc	tctatgatt	attacctcat	ctggccctgg	tttgaacggc	tgaagcaaat	600
gaagttaaat	gagtggttag	accacactcc	aaaactgaaa	ctgtggatgt	cagccatgaa	660
ggaagatccc	acagctccag	cctgctttac	tagtgagaaa	gactggcaag	gtttctcaga	720
gctctactta	cagaacagcc	ctgagggcgt	tgactatggg	ctctgaaggg	ggcaggagtc	780
agcaataaag	ctatgtctga	tattttctct	cactaaaaaa	aaaaaaaaaa	aaactgag	838

<210> 171  
 <211> 547  
 <212> DNA  
 <213> Homo sapien

<400> 171  
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 cttgacaatg cagatcttgc tgaagactct gactggtaag accatcaccc tcgagggttga 120  
 gccacgtgac accatcgaga atgtcaaggc aaagatccaa gataaggaa gcatccctcc 180  
 tgaccagcag aggcgtgatc ttgctggaaa acagctggaa gatggcgca cctgtctctc 240  
 ctacaacatc cagaaagagt ccaccctgca cctggtgctc cgtctcagag gtgggatgca 300  
 aatcttctgt aagacactca ctggcaagac catcacccct gaggtcgagc ccagtgcacac 360  
 catcgagaac gtcaaaagcaa agatccagga caagggaaggc attctctcgt accagcagag 420  
 gttgatcttt gccggaaagc agctggaaga tggggcgacc ctgtctgact acaacatcca 480  
 gaaaagagtct accctgcacc tgggtgctccg tctcagaggt gggatgcaga tcttctgtgaa 540  
 gaccctg 547

<210> 172  
 <211> 608  
 <212> DNA  
 <213> Homo sapien

<400> 172  
 gaattcggca ccagagactt ctccctctga ggctcgca cccctcctca tcagcctgtc 60  
 caccctcatc tacaatggtg ccttgcacat tcagtgcaac cctcaagggt cactgagttc 120  
 tgagtgaac cctcatggtg gtccagtcct gtgcaagcct ggagtggttg ggccgcgtg 180  
 tgacctctgt gccctggtc actatggcct tggcccccaca ggctgtcaag gcgcttgctc 240  
 gggtgctcgt gatcacacag ggggtgagca ctgtgaaagg tgcaattgctg gtttccacgg 300  
 ggaccacagg ctgccatatt ggggccagtg ccggccctgt cctgtcctg aaggccctgg 360  
 gagcaacagg cactttgtcta ctcttggca ccaggatgaa tattcccagc agattgtgtg 420  
 ccactgccgg gcaggtctata cggggctgcg atgtgaagct tgtgccctcg ggcaacttgg 480  
 ggaccatca aggccaggtg gccggtgcca actgtgtgag tgcaatggga acattgaccc 540  
 aatggatcct gatgcctgtg acccccacac ggggcaatgc ctgcgtgtgt tacaccacac 600  
 agagggtc 608

<210> 173  
 <211> 543  
 <212> DNA  
 <213> Homo sapien

<400> 173  
 gaattcggca ccagagatca tccgccagca gggctctggc tctactgact acgtgcgcgc 60  
 ccgctcctac gctgaggacc tgttcaggcc tcggatcctc tctctcgaga cctacaacct 120  
 gctccgggag ggcaccagga gctctcgtga ggctctcgag gcggagtcgc cctgggtgcta 180  
 cctctatggc acgggctcgc tggctggtgt ctacctgcc ggttccaggc agacactgag 240  
 catctaccag gctctcaaga aagggtgctg gactgccgag gtggcccgcc tctgtctgga 300  
 ggcacaggca gccacaggct tctgtctgga ccggtgga ggggaacggc tgaactgtga 360  
 tgaagctgtg cggaaaggcc tctgtggggc cgaactgcac gaccgcctgc tctcggctga 420  
 gcggcggtgc accgcctacc gtgaacccca caaccgagac accatctcgc tcttcagggc 480  
 catgaagaag gaactgatcc ctactgagga ggcctctcgc ctgtggatgc ccagctggcc 540  
 acc 543

<210> 174  
 <211> 548  
 <212> DNA  
 <213> Homo sapien

<400> 174



gaattcggca	cgagaaatgg	cggcaggggt	cgaagcggcg	cgaggaggtg	cggcgacgga	60
gatcaaaatg	gaggaagaga	gcggcgcgcc	cggcgtgccg	agcggcaacg	gggctccggg	120
ccttaagggt	gaaggagaa	gacctgctca	gaatgagaag	aggaaggaga	aaaacataaa	180
aagaggagtc	aatcgctttg	agccatatgc	caatccaact	aaaagatata	gagccttcat	240
tacaaaacata	ccttttgatg	tgaatggca	gtcacttaaa	gacctgggtta	aagaaaaagt	300
tggtgaggtg	acatactggg	agctcttaat	ggacgctgaa	ggaaagtcaa	ggggatgtgc	360
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tagtctgagc	ggaagaccac	tgaagatcct	agaagatcct	gatggtgaac	atgccaggag	480
agcaatgcaa	aaggtgatgg	ctacgactgg	tgggatgggt	atgggaccag	gtggcccagg	540
aatgatta						548

&lt;210&gt; 175

&lt;211&gt; 604

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 175

gaattcggca	ccagaggacc	tccaggacat	gttcatcgtc	cataccatcg	aggagattga	60
gggctgatc	tcagcccatg	accagttcaa	gtccacccgt	ccggacgcgc	ataggggagcg	120
cgaggccatc	ctggccatcc	caaggaggcg	ccagaggatc	gctgagagca	accacatcaa	180
gctgtcgggc	agcaaccocct	acaccacccgt	caccocccaa	atcatcaact	ccaagtggga	240
gaaggtgcag	cagctgggtgc	caaaacggga	ccatgcocct	ctggaggagc	agagcaagca	300
gcagtcacac	gagcacctgc	gccgccagtt	cgccagccag	gccaatgttg	tggggccctg	360
gatccagacc	aagatggagg	agatcggggc	catctccatt	gagatgaacg	ggacccttga	420
ggacacgctg	agccacccga	acaggtatga	acgcagcatc	gtggactaca	agcccaacct	480
ggacctgctg	gagcagcagc	accagcttat	ccaggaggcc	ctcatcttgc	acaacaagca	540
caccaactat	accatggagc	acatccgcgt	gggctgggag	cagctgctca	ccaccattgc	600
ccgg						604

&lt;210&gt; 176

&lt;211&gt; 486

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 176

gaattcggca	ccagccaagc	tcactattga	atccacgcgc	ttcaatgtcg	cagaggggaa	60
ggaggttcct	ctactcgccc	acaacccctgc	ccagaatcgt	attggttaca	gctgggtacaa	120
agggcgaaga	gtggatggca	acagttcaat	tgtaggatat	gtaataggaa	ctcaacaagc	180
taccocaggg	cccgcataca	gtggtcgaga	gacaatatac	cccaatgcat	cctgctgtat	240
ccagaacgtc	accagaaatg	acacaggatt	ctatacccta	caagtataaa	agtcagatct	300
tgtgaatgaa	gaagcaaccg	gacagttcca	tgtatacccg	gagctgccca	agccctccat	360
ctccagcaac	aactccaacc	cgtggaggga	caaggatgct	gtggccttca	cctgtgaacc	420
tgaggttcag	aacacaacct	acctgtgggt	ggtaaatggt	cagagcctcc	cggtcagctc	480
caaggc						486

&lt;210&gt; 177

&lt;211&gt; 387

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 177

gaattcggca	ccagggacag	cagaccagac	agtcacagca	gccttgacaa	aacgttccgt	60
gaactcaagc	tcttctccac	agaggaggag	agagcagaca	gcagagacca	tggagttccc	120
ctcggccccc	cccacagatg	ggtgcattccc	ctggcagagg	ctcctgctca	cagcctcaact	180
tctaaccctc	tggaaaccgc	ccaccactgc	caagctcaact	attgaatcca	cgccgttcaa	240
tgtcgcagag	gggaaggagg	tgcttctaact	tgtccacaat	ctgcccccag	atctttttgg	300
ctacagctgg	tacaaagggt	aaagagtgga	tggcaaccgt	caaatatag	gatatgtaat	360
aggaactcaa	caagctaccc	caggggc				387

<210> 178  
 <211> 440  
 <212> DNA  
 <213> Homo sapien

<400> 178  
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 aagtaaccaa aatgaacctg ttaaatcagc aaatccaaga agaactctct agagttaacca 180  
 aactaaagga gacagcagaa gaagagaaag atgatttgga agagaggctt atgaatcaat 240  
 tagcagaact taatggaagc attgggaatt actgtcagga tgttacagat gcccaataa 300  
 aaaatgagct attggaatct gaaatgaaga accttaaaaa gtgtgtgagt gaattggaag 360  
 aagaaaagca gcagttagtc aaggaaaaaa ctaaggtgga atcagaataa cgaaaggaat 420  
 atttggagaa aatacaagg 440

<210> 179  
 <211> 443  
 <212> DNA  
 <213> Homo sapien

<400> 179  
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 cgggctctgt gcgggcaaac agaagctaac catgcagaac ctcaacgacc gcctggcctc 120  
 ctactctggc aaggtgcgog cctctggaggc ggccaacggc gagctagagg tgaagatccg 180  
 cgactgtgtac cagaagcagg ggcctgggcc ctcccgcgac tacagcactt actacaacgac 240  
 catccaggac ctgcggggaca agattcttgg tgccaccatt gagaactcca ggattgtcct 300  
 gcagatcgac aacgcccgctc tggctgcaga tgacttccga accaagtttg agacggaaca 360  
 ggctctgcgc atgagcgtgg agggccgacat caacggcctg cgcagggtgc tggatgagct 420  
 gacctctggc aggaccgacc tgg 443

<210> 180  
 <211> 403  
 <212> DNA  
 <213> Homo sapien

<400> 180  
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 caaacaacca gaggattaag gctgtgttcc caagcatcaa attctgcttg gacaatggag 120  
 caaagtcggt agtctcttatg agccacctag gccggcctga tgggtgtgcc atgcctgcga 180  
 agtaactcctt agagccagtt gctgtgaaac tcagatctct gctgggcaag gatgttctgt 240  
 tcttgaagga ctgtgttagc ccagaagtgg agaaagcctg tgccaaccca gctgtgggtg 300  
 ctgtcatcct gctggagaac ctccgcttcc atgtggagga agaaggggaag ggaaagatg 360  
 cttctgggaa caaggttaaa gccgagccag ccaaaataga agc 403

<210> 181  
 <211> 493  
 <212> DNA  
 <213> Homo sapien

<400> 181  
 gaattcggca ccagcagagg tctccagagc cttctctctc ctgtgcaaaa tggcaactct 60  
 taaggaaaaa ctcatctgac cagttgcgga agaagaggca acagttccaa acaataagat 120  
 cactgtagtg ggtgttgagc aagttggatg ggcgtgtgct atcagacttc tgggaagtc 180  
 tctggctgat gaacttgctc ttgtggatgt ttgtgaagat aagcttaaa gagaatgat 240  
 ggatctgcag catgggagct taattcttca gacacctaaa attgtggcag ataaagatta 300  
 ttctgtgacc gccaaattcta agattgtagt ggtaaactga ggagtcctgc agcaagaagg 360  
 ggagagtcgg ctcaatctgg tgcagagaaa tgtaaactgc ttcaaatcca ttattcctca 420

gatcgtcaag tacagtctcg attgcatcat aattgtggtt tccaaccagcaggaggacattct 480  
tacgatgtgtt acc 493

<210> 182  
<211> 209  
<212> PRT  
<213> Homo sapien

<400> 182  
Ala Phe Ser Ser Asn Pro Lys Val Gln Val Glu Ala Ile Glu Gly Gly  
1 5 10 15  
Ala Leu Gln Lys Leu Leu Val Ile Leu Ala Thr Glu Gln Pro Leu Thr  
20 25 30  
Ala Lys Lys Lys Val Leu Phe Ala Leu Cys Ser Leu Leu Arg His Phe  
35 40 45  
Pro Tyr Ala Gln Arg Gln Phe Leu Lys Leu Gly Gly Leu Gln Val Leu  
50 55 60  
Arg Thr Leu Val Gln Glu Lys Gly Thr Glu Val Leu Ala Val Arg Val  
65 70 75 80  
Val Thr Leu Leu Tyr Asp Leu Val Thr Glu Lys Met Phe Ala Glu Glu  
85 90 95  
Glu Ala Glu Leu Thr Gln Glu Met Ser Pro Glu Lys Leu Gln Gln Tyr  
100 105 110  
Arg Gln Val His Leu Leu Pro Gly Leu Trp Glu Gln Gly Trp Cys Glu  
115 120 125  
Ile Thr Ala His Leu Leu Ala Leu Pro Glu His Asp Ala Arg Glu Lys  
130 135 140  
Val Leu Gln Thr Leu Gly Val Leu Leu Thr Thr Cys Arg Asp Arg Tyr  
145 150 155 160  
Arg Gln Asp Pro Gln Leu Gly Arg Thr Leu Ala Ser Leu Gln Ala Glu  
165 170 175  
Tyr Gln Val Leu Ala Ser Leu Glu Leu Gln Asp Gly Glu Asp Glu Gly  
180 185 190  
Tyr Phe Gln Glu Leu Leu Gly Ser Val Asn Ser Leu Leu Lys Glu Leu  
195 200 205  
Arg

<210> 183  
<211> 255  
<212> PRT  
<213> Homo sapien

<400> 183  
Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Pro  
1 5 10 15  
Lys Met Glu Glu Glu Ser Gly Ala Pro Cys Val Pro Ser Gly Asn Gly  
20 25 30  
Ala Pro Gly Pro Lys Gly Glu Glu Arg Pro Thr Gln Asn Glu Lys Arg  
35 40 45  
Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr Ser  
50 55 60  
Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe Asp  
65 70 75 80  
Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly Glu  
85 90 95  
Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg Gly  
100 105 110

Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala Ala  
 115 120 125  
 Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val Lys  
 130 135 140  
 Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala Gly  
 145 150 155 160  
 Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val Gly  
 165 170 175  
 Trp Lys Lys Leu Lys Glu Val Phe Ser Met Ala Gly Val Val Val Arg  
 180 185 190  
 Ala Asp Ile Leu Glu Asp Lys Asp Gly Lys Ser Arg Gly Ile Gly Ile  
 195 200 205  
 Val Thr Phe Glu Gln Ser Ile Glu Ala Val Gln Ala Ile Ser Met Phe  
 210 215 220  
 Asn Gly Gln Leu Leu Phe Asp Arg Pro Met His Val Lys Met Asp Glu  
 225 230 235 240  
 Arg Ala Leu Pro Lys Gly Asp Phe Phe Pro Pro Glu Arg His Ser  
 245 250 255

<210> 184  
 <211> 188  
 <212> PRT  
 <213> Homo sapien

<400> 184  
 Leu Ser Gly Ser Cys Ile Arg Arg Glu Gln Thr Pro Glu Lys Glu Lys  
 1 5 10 15  
 Gln Val Val Leu Phe Glu Glu Ala Ser Trp Thr Cys Thr Pro Ala Cys  
 20 25 30  
 Gly Asp Glu Pro Arg Thr Val Ile Leu Leu Ser Ser Met Leu Ala Asp  
 35 40 45  
 His Arg Leu Lys Leu Glu Asp Tyr Lys Asp Arg Leu Lys Ser Gly Glu  
 50 55 60  
 His Leu Asn Pro Asp Gln Leu Glu Ala Val Glu Lys Tyr Glu Glu Val  
 65 70 75 80  
 Leu His Asn Leu Glu Phe Ala Lys Glu Leu Gln Lys Thr Phe Ser Gly  
 85 90 95  
 Leu Ser Leu Asp Leu Leu Lys Ala Gln Lys Lys Ala Gln Arg Arg Glu  
 100 105 110  
 His Met Leu Lys Leu Glu Ala Glu Lys Lys Lys Leu Arg Thr Ile Leu  
 115 120 125  
 Gln Val Gln Tyr Val Leu Gln Asn Leu Thr Gln Glu His Val Gln Lys  
 130 135 140  
 Asp Phe Lys Gly Gly Leu Asn Gly Ala Val Tyr Leu Pro Ser Lys Glu  
 145 150 155 160  
 Leu Asp Tyr Leu Ile Lys Phe Ser Lys Leu Thr Cys Pro Glu Arg Asn  
 165 170 175  
 Glu Ser Leu Arg Gln Thr Leu Glu Gly Ser Thr Val  
 180 185

<210> 185  
 <211> 746  
 <212> PRT  
 <213> Homo sapien

<400> 185  
 Asp Lys His Leu Lys Asp Leu Leu Ser Lys Leu Leu Asn Ser Gly Tyr  
 1 5 10 15

Phe Glu Ser Ile Pro Val Pro Lys Asn Ala Lys Glu Lys Glu Val Pro  
 20 25 30  
 Leu Glu Glu Glu Met Leu Ile Gln Ser Glu Lys Lys Thr Gln Leu Ser  
 35 40 45  
 Lys Thr Glu Ser Val Lys Glu Ser Glu Ser Leu Met Glu Phe Ala Gln  
 50 55 60  
 Pro Glu Ile Gln Pro Gln Glu Phe Leu Asn Arg Arg Tyr Met Thr Glu  
 65 70 75 80  
 Val Asp Tyr Ser Asn Lys Gln Gly Glu Glu Gln Pro Trp Glu Ala Asp  
 85 90 95  
 Tyr Ala Arg Lys Pro Asn Leu Pro Lys Arg Trp Asp Met Leu Thr Glu  
 100 105 110  
 Pro Asp Gly Gln Glu Lys Lys Gln Glu Ser Phe Lys Ser Trp Glu Ala  
 115 120 125  
 Ser Gly Lys His Gln Glu Val Ser Lys Pro Ala Val Ser Leu Glu Gln  
 130 135 140  
 Arg Lys Gln Asp Thr Ser Lys Leu Arg Ser Thr Leu Pro Glu Glu Gln  
 145 150 155 160  
 Lys Lys Gln Glu Ile Ser Lys Ser Lys Pro Ser Pro Ser Gln Trp Lys  
 165 170 175  
 Gln Asp Thr Pro Lys Ser Lys Ala Gly Tyr Val Gln Glu Glu Gln Lys  
 180 185 190  
 Lys Gln Glu Thr Pro Lys Leu Trp Pro Val Gln Leu Gln Lys Glu Gln  
 195 200 205  
 Asp Pro Lys Lys Gln Thr Pro Lys Ser Trp Thr Pro Ser Met Gln Ser  
 210 215 220  
 Glu Gln Asn Thr Thr Lys Ser Trp Thr Thr Pro Met Cys Glu Glu Gln  
 225 230 235 240  
 Asp Ser Lys Gln Pro Glu Thr Pro Lys Ser Trp Glu Asn Asn Val Glu  
 245 250 255  
 Ser Gln Lys His Ser Leu Thr Ser Gln Ser Gln Ile Ser Pro Lys Ser  
 260 265 270  
 Trp Gly Val Ala Thr Ala Ser Leu Ile Pro Asn Asp Gln Leu Leu Pro  
 275 280 285  
 Arg Lys Leu Asn Thr Glu Pro Lys Asp Val Pro Lys Pro Val His Gln  
 290 295 300  
 Pro Val Gly Ser Ser Thr Leu Pro Lys Asp Pro Val Leu Arg Lys  
 305 310 315 320  
 Glu Lys Leu Gln Asp Leu Met Thr Gln Ile Gln Gly Thr Cys Asn Phe  
 325 330 335  
 Met Gln Glu Ser Val Leu Asp Phe Asp Lys Pro Ser Ser Ala Ile Pro  
 340 345 350  
 Thr Ser Gln Pro Pro Ser Ala Thr Pro Gly Ser Pro Val Ala Ser Lys  
 355 360 365  
 Glu Gln Asn Leu Ser Ser Gln Ser Asp Phe Leu Gln Glu Pro Leu Gln  
 370 375 380  
 Val Phe Asn Val Asn Ala Pro Leu Pro Pro Arg Lys Glu Gln Glu Ile  
 385 390 395 400  
 Lys Glu Ser Pro Tyr Ser Pro Gly Tyr Asn Gln Ser Phe Thr Thr Ala  
 405 410 415  
 Ser Thr Gln Thr Thr Pro Pro Gln Cys Gln Leu Pro Ser Ile His Val Glu  
 420 425 430  
 Gln Thr Val His Ser Gln Glu Thr Ala Ala Asn Tyr His Pro Asp Gly  
 435 440 445  
 Thr Ile Gln Val Ser Asn Gly Ser Leu Ala Phe Tyr Pro Ala Gln Thr  
 450 455 460  
 Asn Val Phe Pro Arg Pro Thr Gln Pro Phe Val Asn Ser Arg Gly Ser  
 465 470 475 480

Val	Arg	Gly	Cys	Thr	Arg	Gly	Gly	Arg	Leu	Ile	Thr	Asn	Ser	Tyr	Arg
Ser	Pro	Gly	Gly	485	Tyr	Lys	Gly	Phe	Asp	Thr	Thr	Arg	Gly	Leu	Pro
Ile	Ser	Asn	Gly	500	Asn	Tyr	Ser	Gln	Leu	Gln	Phe	Gln	Ala	Arg	Glu
Ser	Gly	515	Ala	Pro	Tyr	Ser	Gln	Arg	Asp	Asn	Phe	Gln	Gln	Cys	Tyr
Arg	Gly	Gly	Thr	Ser	Gly	Gly	Pro	Arg	Ala	Asn	Ser	Arg	Ala	Gly	Tyr
545	Ser	Asp	Ser	Ser	Gln	Val	Ser	Ser	Pro	Glu	Arg	Asp	Asn	Glu	Thr
Asn	Ser	Gly	Asp	Ser	Gly	Gln	Gly	Asp	Ser	Arg	Ser	Met	Thr	Pro	Val
Asp	Val	Pro	Val	Thr	Asn	Pro	Ala	Ala	Thr	Ile	Leu	Pro	Val	His	Val
Tyr	Pro	Leu	Pro	Gln	Gln	Met	Arg	Val	Ala	Phe	Ser	Ala	Ala	Arg	Thr
610	Ser	Asn	Leu	Ala	Pro	Gly	Thr	Leu	Asp	Gln	Pro	Ile	Val	Phe	Asp
625	Leu	Leu	Asn	Asn	Leu	Gly	Glu	Thr	Phe	Asp	Leu	Gln	Leu	Gly	Arg
Leu	Leu	Asn	Asn	Leu	645	Gly	Glu	Thr	Phe	Asp	Leu	Gln	Leu	Gly	Arg
Asn	Cys	Pro	Val	Asn	Gly	Thr	Tyr	Val	Phe	Ile	Phe	His	Met	Leu	Lys
Leu	Ala	Val	Asn	Val	Pro	Leu	Tyr	Val	Asn	Leu	Met	Lys	Asn	Glu	Glu
Val	Leu	Val	Ser	Ala	Tyr	Ala	Asn	Asp	Gly	Ala	Pro	Asp	His	Glu	Thr
Ala	Ser	Asn	His	Ala	Ile	Leu	Gln	Leu	Phe	Gln	Gly	Asp	Gln	Ile	Trp
705	Leu	Arg	Leu	His	Arg	Gly	Ala	Ile	Tyr	Gly	Ser	Ser	Trp	Lys	Ser
Thr	Phe	Ser	Gly	Tyr	Leu	Leu	Tyr	Gln	Asp						

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<210> 186
<211> 705
<212> PRT
<213> Homo sapien
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<400> 186																	
1	Ala	Leu	Leu	Asn	Val	Arg	Gln	Pro	Pro	Ser	Thr	Thr	Thr	Phe	Val	Leu	
	Asn	Gln	Ile	Asn	His	Leu	Pro	Pro	Leu	Gly	Ser	Thr	Ile	Val	Met	Thr	
				20					25					30			
Lys	Thr	Pro	Pro	Val	Thr	Thr	Asn	Arg	Gln	Thr	Ile	Thr	Leu	Thr	Lys		
		35					40					45					
Phe	Ile	Gln	Thr	Thr	Ala	Ser	Thr	Arg	Pro	Ser	Val	Ser	Ala	Pro	Thr		
	50					55					60						
Val	Arg	Asn	Ala	Met	Thr	Ser	Ala	Pro	Ser	Lys	Asp	Gln	Val	Gln	Leu	80	
65					70					75							
Lys	Asp	Leu	Leu	Lys	Asn	Asn	Ser	Leu	Asn	Glu	Leu	Met	Lys	Leu	Lys		
				85					90					95			
Pro	Pro	Ala	Asn	Ile	Ala	Gln	Pro	Val	Ala	Thr	Ala	Ala	Thr	Asp	Val		
			100					105					110				
Ser	Asn	Gly	Thr	Val	Lys	Lys	Glu	Ser	Ser	Asn	Lys	Glu	Gly	Ala	Arg		
		115					120					125					
Met	Trp	Ile	Asn	Asp	Met	Lys	Met	Arg	Ser	Phe	Ser	Pro	Thr	Met	Lys		

130		135		140
Val Pro Val Val Lys Glu Asp Asp Glu Pro Glu Glu Glu Asp Glu Glu				
145		150		155
Glu Met Gly His Ala Glu Thr Tyr Ala Glu Tyr Met Pro Ile Lys Leu				160
		165		170
Lys Ile Gly Leu Arg His Pro Asp Ala Val Val Glu Thr Ser Ser Leu				175
		180		185
Ser Ser Val Thr Pro Pro Asp Val Trp Tyr Lys Thr Ser Ile Ser Glu				190
		195		200
Glu Thr Ile Asp Asn Gly Trp Leu Ser Ala Leu Gln Leu Glu Ala Ile				205
		210		215
Thr Tyr Ala Ala Gln Gln His Glu Thr Phe Leu Pro Asn Gly Asp Arg				220
225		230		235
Ala Gly Phe Leu Ile Gly Asp Gly Ala Gly Val Gly Lys Gly Arg Thr				240
		245		250
Ile Ala Gly Ile Ile Tyr Glu Asn Tyr Leu Leu Ser Arg Lys Arg Ala				255
		260		265
Leu Trp Phe Ser Val Ser Asn Asp Leu Lys Tyr Asp Ala Glu Arg Asp				270
		275		280
Leu Arg Asp Ile Gly Ala Lys Asn Ile Leu Val His Ser Leu Asn Lys				285
		290		295
Phe Lys Tyr Gly Lys Ile Ser Ser Lys His Asn Gly Ser Val Lys Lys				300
305		310		315
Gly Val Ile Phe Ala Thr Tyr Ser Ser Leu Ile Gly Glu Ser Gln Ser				320
		325		330
Gly Gly Lys Tyr Lys Thr Arg Leu Lys Gln Leu Leu His Trp Cys Gly				335
		340		345
Asp Asp Phe Asp Gly Val Ile Val Phe Asp Glu Cys His Lys Ala Lys				350
		355		360
Asn Leu Cys Pro Val Gly Ser Ser Lys Pro Thr Lys Thr Gly Leu Ala				365
		370		375
Val Leu Glu Leu Gln Asn Lys Leu Pro Lys Ala Arg Val Val Tyr Ala				380
385		390		395
Ser Ala Thr Gly Ala Ser Glu Pro Arg Asn Met Ala Tyr Met Asn Arg				400
		405		410
Leu Gly Ile Trp Gly Glu Gly Thr Pro Phe Arg Glu Phe Ser Asp Phe				415
		420		425
Ile Gln Ala Val Glu Arg Arg Gly Val Gly Ala Met Glu Ile Val Ala				430
		435		440
Met Asp Met Lys Leu Arg Gly Met Tyr Ile Ala Arg Gln Leu Ser Phe				445
		450		455
Thr Gly Val Thr Phe Lys Ile Glu Glu Val Leu Leu Ser Gln Ser Tyr				460
465		470		475
Val Lys Met Tyr Asn Lys Ala Val Lys Leu Trp Val Ile Ala Arg Glu				480
		485		490
Arg Phe Gln Gln Ala Ala Asp Leu Ile Asp Ala Glu Gln Arg Met Lys				495
		500		505
Lys Ser Met Trp Gly Gln Phe Trp Ser Ala His Gln Arg Phe Phe Lys				510
		515		520
Tyr Leu Cys Ile Ala Ser Lys Val Lys Arg Val Val Gln Leu Ala Arg				525
		530		535
Glu Glu Ile Lys Asn Gly Lys Cys Val Val Ile Gly Leu Gln Ser Thr				540
545		550		555
Gly Glu Ala Arg Thr Leu Glu Ala Leu Glu Glu Gly Gly Gly Glu Leu				560
		565		570
Asn Asp Phe Val Ser Thr Ala Lys Gly Val Leu Gln Ser Leu Ile Glu				575
		580		585
Lys His Phe Pro Ala Pro Asp Arg Lys Lys Leu Tyr Ser Leu Leu Gly				590

595 600 605  
 Ile Asp Leu Thr Ala Pro Ser Asn Asn Ser Ser Pro Arg Asp Ser Pro  
 610 615 620  
 Cys Lys Glu Asn Lys Ile Lys Lys Arg Lys Gly Glu Ile Thr Arg  
 625 630 635 640  
 Glu Ala Lys Lys Ala Arg Lys Val Gly Gly Leu Thr Gly Ser Ser Ser  
 645 650 655  
 Asp Asp Ser Gly Ser Glu Ser Asp Ala Ser Asp Asn Glu Glu Ser Asp  
 660 665 670  
 Tyr Glu Ser Ser Lys Asn Met Ser Ser Gly Asp Asp Asp Phe Asn  
 675 680 685  
 Pro Phe Leu Asp Glu Ser Asn Glu Asp Asp Glu Asn Asp Pro Trp Leu  
 690 695 700  
 Ile  
 705

<210> 187  
 <211> 595  
 <212> PRT  
 <213> Homo sapien

<400> 187  
 Glu Ser Pro Arg His Arg Gly Glu Gly Gly Gly Glu Trp Gly Pro Gly  
 1 5 10 15  
 Val Pro Arg Glu Arg Arg Glu Ser Ala Gly Glu Trp Gly Ala Asp Thr  
 20 25 30  
 Pro Lys Glu Gly Gly Glu Ser Ala Gly Glu Trp Gly Ala Glu Val Pro  
 35 40 45  
 Arg Gly Arg Gly Glu Gly Ala Gly Glu Trp Gly Pro Asp Thr Pro Lys  
 50 55 60  
 Glu Arg Gly Gln Gly Val Arg Glu Trp Gly Pro Glu Ile Pro Gln Glu  
 65 70 75 80  
 His Gly Glu Ala Thr Arg Asp Trp Ala Leu Glu Ser Pro Arg Ala Leu  
 85 90 95  
 Gly Glu Asp Ala Arg Glu Leu Gly Ser Ser Pro His Asp Arg Gly Ala  
 100 105 110  
 Ser Pro Arg Asp Leu Ser Gly Glu Ser Pro Cys Thr Gln Arg Ser Gly  
 115 120 125  
 Leu Leu Pro Glu Arg Arg Gly Asp Ser Pro Trp Pro Pro Trp Pro Ser  
 130 135 140  
 Pro Gln Glu Arg Asp Ala Gly Thr Arg Asp Arg Glu Glu Ser Pro Arg  
 145 150 155 160  
 Asp Trp Gly Gly Ala Glu Ser Pro Arg Gly Trp Glu Ala Gly Pro Arg  
 165 170 175  
 Glu Trp Gly Pro Ser Pro Ser Gly His Gly Asp Gly Pro Arg Arg Arg  
 180 185 190  
 Pro Arg Lys Arg Arg Gly Arg Lys Gly Arg Met Gly Arg Gln His Glu  
 195 200 205  
 Ala Ala Ala Thr Ala Ala Thr Ala Thr Ala Thr Gly Gly Thr Ala  
 210 215 220  
 Glu Glu Ala Gly Ala Ser Ala Pro Glu Ser Gln Ala Gly Gly Gly Pro  
 225 230 235 240  
 Arg Gly Arg Ala Arg Gly Pro Arg Gln Gln Gly Arg Arg Arg His Gly  
 245 250 255  
 Thr Gln Arg Arg Arg Gly Pro Pro Gln Ala Arg Glu Glu Gly Pro Arg  
 260 265 270  
 Asp Ala Thr Thr Ile Leu Gly Leu Gly Thr Pro Ser Gly Glu Gln Arg  
 275 280 285



Ala Asp Gln Ser Gln Ala Leu Pro Ala Leu Ala Gly Ala Ala Ala Ala  
 290 295 300  
 His Ala His Ala Ile Pro Gly Ala Gly Pro Ala Ala Pro Val Gly  
 305 310 315 320  
 Gly Arg Gly Arg Arg Gly Gly Trp Arg Gly Arg Arg Gly Gly Ser  
 325 330 335  
 Ala Gly Ala Gly Gly Gly Gly Arg Gly Arg Gly Arg Gly Arg Gly  
 340 345 350  
 Gly Gly Arg Gly Gly Gly Gly Ala Gly Arg Gly Gly Gly Ala Ala Gly  
 355 360 365  
 Pro Arg Glu Gly Ala Ser Ser Pro Gly Ala Arg Arg Gly Glu Gln Arg  
 370 375 380  
 Arg Arg Gly Arg Gly Pro Pro Ala Ala Gly Ala Ala Gln Val Ser Ala  
 385 390 395 400  
 Arg Gly Arg Arg Ala Arg Gly Gln Arg Ala Gly Glu Glu Ala Gln Asp  
 405 410 415  
 Gly Leu Leu Pro Arg Gly Arg Asp Arg Leu Pro Leu Arg Pro Gly Asp  
 420 425 430  
 Ala Asn Gln Arg Ala Glu Arg Pro Gly Pro Pro Arg Gly Gly His Gly  
 435 440 445  
 Pro Val Asn Ala Ser Ser Ala Pro Asp Thr Ser Pro Pro Arg His Pro  
 450 455 460  
 Arg Arg Trp Val Ser Gln Gln Arg Gln Arg Leu Trp Arg Gln Phe Arg  
 465 470 475 480  
 Val Gly Gly Gly Phe Pro Pro Pro Pro Ser Arg Pro Pro Ala Val  
 485 490 495  
 Leu Leu Pro Leu Leu Arg Leu Ala Cys Ala Gly Asp Pro Gly Ala Thr  
 500 505 510  
 Arg Pro Gly Pro Arg Arg Pro Ala Arg Arg Pro Arg Gly Glu Leu Ile  
 515 520 525  
 Pro Arg Arg Pro Asp Pro Ala Ala Pro Ser Glu Glu Gly Leu Arg Met  
 530 535 540  
 Glu Ser Ser Val Asp Asp Gly Ala Thr Ala Thr Thr Ala Asp Ala Ala  
 545 550 555 560  
 Ser Gly Glu Ala Pro Glu Ala Gly Pro Ser Pro Ser His Ser Pro Thr  
 565 570 575  
 Met Cys Gln Thr Gly Gly Pro Gly Pro Pro Pro Gln Pro Pro Arg  
 580 585 590  
 Trp Leu Pro  
 595

&lt;210&gt; 188

&lt;211&gt; 376

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 188

Glu Met Arg Lys Phe Asp Val Pro Ser Met Glu Ser Thr Leu Asn Gln  
 1 5 10 15  
 Pro Ala Met Leu Glu Thr Leu Tyr Ser Asp Pro His Tyr Arg Ala His  
 20 25 30  
 Phe Pro Asn Pro Arg Pro Asp Thr Asn Lys Asp Val Tyr Lys Val Leu  
 35 40 45  
 Pro Glu Ser Lys Lys Ala Pro Gly Ser Gly Ala Val Phe Glu Arg Asn  
 50 55 60  
 Gly Pro His Ala Ser Ser Gly Val Leu Pro Leu Gly Leu Gln Pro  
 65 70 75 80  
 Ala Pro Gly Leu Ser Lys Ser Leu Ser Ser Gln Val Trp Gln Pro Ser



Val His Leu Thr Asp Gly Ile Trp Ser Gln Ile Lys Ser Ala Gly Ser  
 115 120 125  
 Ala Leu Tyr Ala Ser Arg Leu Tyr Leu Ser Arg Tyr Gln Asp Thr His  
 130 135 140  
 Pro Glu Arg Leu Ala Lys His Thr Pro Gly Gly Pro Trp Ile Arg Gly  
 145 150 155 160

<210> 190  
 <211> 146  
 <212> PRT  
 <213> Homo sapien

<400> 190  
 Met Asp Pro Arg Ala Ser Leu Leu Leu Gly Asn Val Tyr Ile His  
 1 5 10 15  
 Pro Thr Ala Lys Val Ala Pro Ser Ala Val Leu Gly Pro Asn Val Ser  
 20 25 30  
 Ile Gly Lys Gly Val Thr Val Gly Glu Gly Val Arg Leu Arg Glu Ser  
 35 40 45  
 Ile Val Leu His Gly Ala Thr Leu Gln Glu His Thr Cys Val Leu His  
 50 55 60  
 Ser Ile Val Gly Trp Gly Ser Thr Val Gly Arg Trp Ala Arg Val Glu  
 65 70 75 80  
 Gly Thr Pro Ser Asp Pro Asn Pro Asn Asp Pro Arg Ala Arg Met Asp  
 85 90 95  
 Ser Glu Ser Leu Phe Lys Asp Gly Lys Leu Leu Pro Ala Ile Thr Ile  
 100 105 110  
 Leu Gly Cys Arg Val Arg Ile Pro Ala Glu Val Leu Ile Leu Asn Ser  
 115 120 125  
 Ile Val Leu Pro His Lys Glu Leu Ser Arg Ser Phe Thr Asn Gln Ile  
 130 135 140  
 Ile Leu  
 145

<210> 191  
 <211> 704  
 <212> PRT  
 <213> Homo sapien

<400> 191  
 Glu Gly Gly Cys Ala Ala Gly Arg Gly Arg Glu Leu Glu Pro Glu Leu  
 1 5 10 15  
 Glu Pro Gly Pro Gly Pro Gly Ser Ala Leu Glu Pro Gly Glu Glu Phe  
 20 25 30  
 Glu Ile Val Asp Arg Ser Gln Leu Pro Gly Pro Gly Asp Leu Arg Ser  
 35 40 45  
 Ala Thr Arg Pro Arg Ala Ala Glu Gly Trp Ser Ala Pro Ile Leu Thr  
 50 55 60  
 Leu Ala Arg Arg Ala Thr Gly Asn Leu Ser Ala Ser Cys Gly Ser Ala  
 65 70 75 80  
 Leu Arg Ala Ala Ala Gly Leu Gly Gly Asp Ser Gly Asp Gly Thr  
 85 90 95  
 Ala Arg Ala Ala Ser Lys Cys Gln Met Met Glu Glu Arg Ala Asn Leu  
 100 105 110  
 Met His Met Met Lys Leu Ser Ile Lys Val Leu Leu Gln Ser Ala Leu  
 115 120 125  
 Ser Leu Gly Arg Ser Leu Asp Ala Asp His Ala Pro Leu Gln Gln Phe  
 130 135 140

Phe Val Val Met Glu His Cys Leu Lys His Gly Leu Lys Val Lys Lys  
 145 150 155 160  
 Ser Phe Ile Gly Gln Asn Lys Ser Phe Phe Gly Pro Leu Glu Leu Val  
 165 170 175  
 Glu Lys Leu Cys Pro Glu Ala Ser Asp Ile Ala Thr Ser Val Arg Asn  
 180 185 190  
 Leu Pro Glu Leu Lys Thr Ala Val Gly Arg Gly Arg Ala Trp Leu Tyr  
 195 200 205  
 Leu Ala Leu Met Gln Lys Lys Leu Ala Asp Tyr Leu Lys Val Leu Ile  
 210 215 220  
 Asp Asn Lys His Leu Leu Ser Glu Phe Tyr Glu Pro Glu Ala Leu Met  
 225 230 235 240  
 Met Glu Glu Glu Gly Met Val Ile Val Gly Leu Val Gly Leu Asn  
 245 250 255  
 Val Leu Asp Ala Asn Leu Cys Leu Lys Gly Glu Asp Leu Asp Ser Gln  
 260 265 270  
 Val Gly Val Ile Asp Phe Ser Leu Tyr Leu Lys Asp Val Gln Asp Leu  
 275 280 285  
 Asp Gly Gly Lys Glu His Glu Arg Ile Thr Asp Val Leu Asp Gln Lys  
 290 295 300  
 Asn Tyr Val Glu Glu Leu Asn Arg His Leu Ser Cys Thr Val Gly Asp  
 305 310 315 320  
 Leu Gln Thr Lys Ile Asp Gly Leu Glu Lys Thr Asn Ser Lys Leu Gln  
 325 330 335  
 Glu Glu Leu Ser Ala Ala Thr Asp Arg Ile Cys Ser Leu Gln Glu Glu  
 340 345 350  
 Gln Gln Gln Leu Arg Glu Gln Asn Glu Leu Ile Arg Glu Arg Ser Glu  
 355 360 365  
 Lys Ser Val Glu Ile Thr Lys Gln Asp Thr Lys Val Glu Leu Glu Thr  
 370 375 380  
 Tyr Lys Gln Thr Arg Gln Gly Leu Asp Glu Met Tyr Ser Asp Val Trp  
 385 390 395 400  
 Lys Gln Leu Lys Glu Glu Lys Lys Val Arg Leu Glu Leu Glu Lys Glu  
 405 410 415  
 Leu Glu Leu Gln Ile Gly Met Lys Thr Glu Met Glu Ile Ala Met Lys  
 420 425 430  
 Leu Leu Glu Lys Asp Thr His Glu Lys Gln Asp Thr Leu Val Ala Leu  
 435 440 445  
 Arg Gln Gln Leu Glu Glu Val Lys Ala Ile Asn Leu Gln Met Phe His  
 450 455 460  
 Lys Ala Gln Asn Ala Glu Ser Ser Leu Gln Gln Lys Asn Glu Ala Ile  
 465 470 475 480  
 Thr Ser Phe Glu Gly Lys Thr Asn Gln Val Met Ser Ser Met Lys Gln  
 485 490 495  
 Met Glu Glu Arg Leu Gln His Ser Glu Arg Ala Arg Gln Gly Ala Glu  
 500 505 510  
 Glu Arg Ser His Lys Leu Gln Gln Glu Leu Gly Gly Arg Ile Gly Ala  
 515 520 525  
 Leu Gln Leu Gln Leu Ser Gln Leu His Glu Gln Cys Ser Ser Leu Glu  
 530 535 540  
 Lys Glu Leu Lys Ser Glu Lys Glu Gln Arg Gln Ala Leu Gln Arg Glu  
 545 550 555 560  
 Leu Gln His Glu Lys Asp Thr Ser Ser Leu Leu Arg Met Glu Leu Gln  
 565 570 575  
 Gln Val Glu Gly Leu Lys Lys Glu Leu Arg Glu Leu Gln Asp Glu Lys  
 580 585 590  
 Ala Glu Leu Gln Lys Ile Cys Glu Glu Gln Glu Gln Ala Leu Gln Glu  
 595 600 605

Met Gly Leu His Leu Ser Gln Ser Lys Leu Lys Met Glu Asp Ile Lys  
 610 615 620  
 Glu Val Asn Gln Ala Leu Lys Gly His Ala Trp Leu Lys Asp Asp Glu  
 625 630 635 640  
 Ala Thr His Cys Arg Gln Cys Glu Lys Glu Phe Ser Ile Ser Arg Arg  
 645 650 655  
 Lys His His Cys Arg Asn Cys Gly His Ile Phe Cys Asn Thr Cys Ser  
 660 665 670  
 Ser Asn Glu Leu Ala Leu Pro Ser Tyr Pro Lys Pro Val Arg Val Cys  
 675 680 685  
 Asp Ser Cys His Thr Leu Leu Leu Gln Arg Cys Ser Ser Thr Ala Ser  
 690 695 700

&lt;210&gt; 192

&lt;211&gt; 331

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 192

Arg Ala Gly Ala Ser Ala Met Ala Leu Arg Lys Glu Leu Leu Lys Ser  
 1 5 10 15  
 Ile Trp Tyr Ala Phe Thr Ala Leu Asp Val Glu Lys Ser Gly Lys Val  
 20 25 30  
 Ser Lys Ser Gln Leu Lys Val Leu Ser His Asn Leu Tyr Thr Val Leu  
 35 40 45  
 His Ile Pro His Asp Pro Val Ala Leu Glu Glu His Phe Arg Asp Asp  
 50 55 60  
 Asp Asp Gly Pro Val Ser Ser Gln Gly Tyr Met Pro Tyr Leu Asn Lys  
 65 70 75 80  
 Tyr Ile Leu Asp Lys Val Glu Glu Gly Ala Phe Val Lys Glu His Phe  
 85 90 95  
 Asp Glu Leu Cys Trp Thr Leu Thr Ala Lys Lys Asn Tyr Arg Ala Asp  
 100 105 110  
 Ser Asn Gly Asn Ser Met Leu Ser Asn Gln Asp Ala Phe Arg Leu Trp  
 115 120 125  
 Cys Leu Phe Asn Phe Leu Ser Glu Asp Lys Tyr Pro Leu Ile Met Val  
 130 135 140  
 Pro Asp Glu Val Glu Tyr Leu Leu Lys Lys Val Leu Ser Ser Met Ser  
 145 150 155 160  
 Leu Glu Val Ser Leu Gly Glu Leu Glu Glu Leu Leu Ala Gln Glu Ala  
 165 170 175  
 Gln Val Ala Gln Thr Thr Gly Gly Leu Ser Val Trp Gln Phe Leu Glu  
 180 185 190  
 Leu Phe Asn Ser Gly Arg Cys Leu Arg Gly Val Gly Arg Asp Thr Leu  
 195 200 205  
 Ser Met Ala Ile His Glu Val Tyr Gln Glu Leu Ile Gln Asp Val Leu  
 210 215 220  
 Lys Gln Gly Tyr Leu Trp Lys Arg Gly His Leu Arg Arg Asn Trp Ala  
 225 230 235 240  
 Glu Arg Trp Phe Gln Leu Gln Pro Ser Cys Leu Cys Tyr Phe Gly Ser  
 245 250 255  
 Glu Glu Cys Lys Glu Lys Arg Gly Ile Ile Pro Leu Asp Ala His Cys  
 260 265 270  
 Cys Val Glu Val Leu Pro Asp Arg Asp Gly Lys Arg Cys Met Phe Cys  
 275 280 285  
 Val Lys Thr Ala Thr Arg Thr Tyr Glu Met Ser Ala Ser Asp Thr Arg  
 290 295 300  
 Gln Arg Gln Glu Trp Thr Ala Ala Ile Gln Met Ala Ile Arg Leu Gln

005	310										315										320																		
Ala	Glu	Gly	Lys	Thr	Ser	Leu	His	Lys	Asp	Leu																													
					325																330																		
																				<210> 193																			
																				<211> 475																			
																				<212> PRT																			
																				<213> Homo sapien																			
																				<400> 193																			
Lys	Asn	Ser	Pro	Leu	Ser	Val	Ser	Ser	Gln	Thr	Ile	Thr	Lys	Glu																									
1					5																10					15													
Asn	Asn	Arg	Asn	Val	His	Leu	Glu	His	Ser	Glu	Gln	Asn	Pro	Gly	Ser																								
				20																25					30														
Ser	Ala	Gly	Asp	Thr	Ser	Ala	Ala	His	Gln	Val	Val	Leu	Gly	Glu	Asn																								
				35																40					45														
Leu	Ile	Ala	Thr	Ala	Leu	Cys	Leu	Ser	Gly	Ser	Gly	Ser	Gln	Ser	Asp																								
				50																55					60														
Leu	Lys	Asp	Val	Ala	Ser	Thr	Ala	Gly	Glu	Glu	Gly	Asp	Thr	Ser	Leu																								
				65																70					75														
Arg	Glu	Ser	Leu	His	Pro	Val	Thr	Arg	Ser	Leu	Lys	Ala	Gly	Cys	His																								
				85																90					95														
Thr	Lys	Gln	Leu	Ala	Ser	Arg	Asn	Cys	Ser	Glu	Glu	Lys	Ser	Pro	Gln																								
				100																105					110														
Thr	Ser	Ile	Leu	Lys	Glu	Gly	Asn	Arg	Asp	Thr	Ser	Leu	Asp	Phe	Arg																								
				115																120					125														
Pro	Val	Val	Ser	Pro	Ala	Asn	Gly	Val	Glu	Gly	Val	Arg	Val	Asp	Gln																								
				130																135					140														
Asp	Asp	Asp	Gln	Asp	Ser	Ser	Ser	Leu	Lys	Leu	Ser	Gln	Asn	Ile	Ala																								
				145																150					155														
Val	Gln	Thr	Asp	Phe	Lys	Thr	Ala	Asp	Ser	Glu	Val	Asn	Thr	Asp	Gln																								
				165																170					175														
Asp	Ile	Glu	Lys	Asn	Leu	Asp	Lys	Met	Met	Thr	Glu	Arg	Thr	Leu	Leu																								
				180																185					190														
Lys	Glu	Arg	Tyr	Gln	Glu	Val	Leu	Asp	Lys	Gln	Arg	Gln	Val	Glu	Asn																								
				195																200					205														
Gln	Leu	Gln	Val	Gln	Leu	Lys	Gln	Leu	Gln	Gln	Arg	Arg	Glu	Glu	Glu																								
				210																215					220														
Met	Lys	Asn	His	Gln	Glu	Ile	Leu	Lys	Ala	Ile	Gln	Asp	Val	Thr	Ile																								
				225																230					235														
Lys	Arg	Glu	Glu	Thr	Lys	Lys	Lys	Ile	Glu	Lys	Glu	Lys	Lys	Glu	Phe																								
				245																250					255														
Leu	Gln	Lys	Glu	Gln	Asp	Leu	Lys	Ala	Glu	Ile	Glu	Lys	Lys	Cys	Glu																								
				260																265					270														
Lys	Gly	Arg	Arg	Glu	Val	Trp	Glu	Met	Glu	Leu	Asp	Arg	Leu	Lys	Asn																								
				275																280					285														
Gln	Asp	Gly	Glu	Ile	Asn	Arg	Asn	Ile	Met	Glu	Glu	Thr	Glu	Arg	Ala																								
				290																295					300														
Trp	Lys	Ala	Glu	Ile	Leu	Ser	Leu	Glu	Ser	Arg	Lys	Glu	Leu	Leu	Val																								
				305																310					315														
Leu	Lys	Leu	Glu	Glu	Ala	Glu	Lys	Glu	Ala	Glu	Leu	His	Leu	Thr	Tyr																								
				325																330					335														
Leu	Lys	Ser	Thr	Pro	Pro	Thr	Leu	Glu	Thr	Val	Arg	Ser</																											

Ser Ser Leu Pro Gln Ile Pro Thr Pro Thr Leu Pro Pro Pro Pro Ser  
 385 390  
 Glu Thr Asp Phe Met Leu Gln Val Phe Gln Pro Ser Pro Ser Leu Ala  
 405 410  
 Pro Arg Met Pro Phe Ser Ile Gly Gln Val Thr Met Pro Met Val Met  
 420 425 430  
 Pro Ser Ala Asp Pro Arg Ser Leu Ser Phe Pro Ile Leu Asn Pro Ala  
 435 440 445  
 Leu Ser Gln Pro Ser Gln Pro Ser Ser Pro Leu Pro Gly Ser His Gly  
 450 455 460  
 Arg Asn Ser Pro Gly Leu Gly Ser Leu Val Ser  
 465 470 475

<210> 194  
 <211> 241  
 <212> PRT  
 <213> Homo sapien

<400> 194  
 Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro  
 1 5 10 15  
 Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys  
 20 25 30  
 Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg  
 35 40 45  
 His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe  
 50 55 60  
 Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly  
 65 70 75 80  
 Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala  
 85 90 95  
 Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys  
 100 105 110  
 Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly  
 115 120 125  
 Ser Phe Ile Arg Ser Gln Asn Lys Glu Asp Tyr Ala Gly Leu Lys Glu  
 130 135 140  
 Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Val Leu Thr Asn Lys  
 145 150 155 160  
 Lys Thr Thr Phe Phe Gly Gly Asn Ser Ile Ser Met Ile Asp Tyr Leu  
 165 170 175  
 Ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys  
 180 185 190  
 Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu  
 195 200 205  
 Asp Pro Thr Val Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly  
 210 215 220  
 Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly  
 225 230 235 240  
 Leu

<210> 195  
 <211> 138  
 <212> PRT  
 <213> Homo sapien

<400> 195

Gln Thr Lys Ile Leu Glu Glu Asp Leu Glu Gln Ile Lys Leu Ser Leu  
 1 5 10 15  
 Arg Glu Arg Gly Arg Glu Leu Thr Thr Gln Arg Gln Leu Met Gln Glu  
 20 25 30  
 Arg Ala Glu Glu Gly Lys Gly Pro Ser Lys Ala Gln Arg Gly Ser Leu  
 35 40 45  
 Glu His Met Lys Leu Ile Leu Arg Asp Lys Glu Lys Glu Val Glu Cys  
 50 55 60  
 Gln Gln Glu His Ile His Glu Leu Gln Glu Leu Lys Asp Gln Leu Glu  
 65 70 75 80  
 Gln Gln Leu Gln Gly Leu His Arg Lys Val Gly Glu Thr Ser Leu Leu  
 85 90 95  
 Leu Ser Gln Arg Glu Gln Glu Ile Val Val Leu Gln Gln Gln Leu Gln  
 100 105 110  
 Glu Ala Arg Glu Gln Gly Glu Leu Lys Glu Gln Ser Leu Gln Ser Gln  
 115 120 125  
 Leu Asp Glu Ala Gln Arg Ala Leu Ala Gln  
 130 135

<210> 196  
 <211> 102  
 <212> PRT  
 <213> Homo sapien

<400> 196  
 Met Ser Lys Arg Lys Ala Pro Gln Glu Thr Leu Asn Gly Gly Ile Thr  
 1 5 10 15  
 Asp Met Leu Thr Glu Leu Ala Asn Phe Glu Lys Asn Val Ser Gln Ala  
 20 25 30  
 Ile His Lys Tyr Asn Ala Tyr Arg Lys Ala Ala Ser Val Ile Ala Lys  
 35 40 45  
 Tyr Pro His Lys Ile Lys Ser Gly Ala Glu Ala Lys Lys Leu Pro Gly  
 50 55 60  
 Val Gly Thr Lys Ile Ala Glu Lys Ile Asp Glu Phe Leu Ala Thr Gly  
 65 70 75 80  
 Lys Leu Arg Lys Leu Glu Lys Ile Arg Gln Asp Asp Thr Ser Ser Ser  
 85 90 95  
 Ile Asn Phe Leu Thr Arg  
 100

<210> 197  
 <211> 138  
 <212> PRT  
 <213> Homo sapien

<400> 197  
 Glu Ala Asn Glu Val Thr Asp Ser Ala Tyr Met Gly Ser Glu Ser Thr  
 1 5 10 15  
 Tyr Ser Glu Cys Glu Thr Phe Thr Asp Glu Asp Thr Ser Thr Leu Val  
 20 25 30  
 His Pro Glu Leu Gln Pro Glu Gly Asp Ala Asp Ser Ala Gly Gly Ser  
 35 40 45  
 Ala Val Pro Ser Glu Cys Leu Asp Ala Met Glu Glu Pro Asp His Gly  
 50 55 60  
 Ala Leu Leu Leu Leu Pro Gly Arg Pro His Pro His Gly Gln Ser Val  
 65 70 75 80  
 Ile Thr Val Ile Gly Gly Glu Glu His Phe Glu Asp Tyr Gly Glu Gly  
 85 90 95



Ser Glu Ala Glu Leu Ser Pro Glu Thr Leu Cys Asn Gly Gln Leu Gly  
 100 105 110  
 Cys Ser Asp Pro Ala Phe Leu Thr Pro Ser Pro Thr Lys Arg Leu Ser  
 115 120 125  
 Ser Lys Lys Val Ala Arg Tyr Leu His Gln  
 130 135

<210> 198  
 <211> 100  
 <212> PRT  
 <213> Homo sapien

<400> 198  
 Met Gly Asp Val Lys Asn Phe Leu Tyr Ala Trp Cys Gly Lys Arg Lys  
 1 5 10 15  
 Met Thr Pro Ser Tyr Glu Ile Arg Ala Val Gly Asn Lys Asn Arg Gln  
 20 25 30  
 Lys Phe Met Cys Glu Val Gln Val Glu Gly Tyr Asn Tyr Thr Gly Met  
 35 40 45  
 Gly Asn Ser Thr Asn Lys Lys Asp Ala Gln Ser Asn Ala Ala Arg Asp  
 50 55 60  
 Phe Val Asn Tyr Leu Val Arg Ile Asn Glu Ile Lys Ser Glu Glu Val  
 65 70 75 80  
 Pro Ala Phe Gly Val Ala Ser Pro Pro Pro Leu Thr Asp Thr Pro Asp  
 85 90 95  
 Thr Thr Ala Asn  
 100

<210> 199  
 <211> 127  
 <212> PRT  
 <213> Homo sapien

<400> 199  
 Met Val Lys Glu Thr Thr Tyr Tyr Asp Val Leu Gly Val Lys Pro Asn  
 1 5 10 15  
 Ala Thr Gln Glu Glu Leu Lys Lys Ala Tyr Arg Lys Leu Ala Leu Lys  
 20 25 30  
 Tyr His Pro Asp Lys Asn Pro Asn Glu Gly Glu Lys Phe Lys Gln Ile  
 35 40 45  
 Ser Gln Ala Tyr Glu Val Leu Ser Asp Ala Lys Lys Arg Glu Leu Tyr  
 50 55 60  
 Asp Lys Gly Gly Glu Gln Ala Ile Lys Glu Gly Gly Ala Gly Gly Gly  
 65 70 75 80  
 Phe Gly Ser Pro Met Asp Ile Phe Asp Met Phe Phe Gly Gly Gly Gly  
 85 90 95  
 Arg Met Gln Arg Glu Arg Arg Gly Lys Asn Val Val His Gln Leu Ser  
 100 105 110  
 Val Thr Leu Glu Asp Leu Tyr Asn Gly Ala Thr Arg Lys Leu Ala  
 115 120 125

<210> 200  
 <211> 90  
 <212> PRT  
 <213> Homo sapien

<400> 200  
 Met Ala Cys Pro Leu Asp Gln Ala Ile Gly Leu Leu Val Ala Ile Phe

1	5	10	15
His Lys Tyr Ser Gly Arg Glu Gly Asp Lys His Thr Leu Ser Lys Lys	20	25	30
Glu Leu Lys Glu Leu Ile Gln Lys Glu Leu Thr Ile Gly Ser Lys Leu	35	40	45
Gln Asp Ala Glu Ile Ala Arg Leu Met Glu Asp Leu Asp Arg Asn Lys	50	55	60
Asp Gln Glu Val Asn Phe Gln Glu Tyr Val Thr Phe Leu Gly Ala Leu	65	70	75
Ala Leu Ile Tyr Asn Glu Ala Leu Lys Gly	85	90	80

<210> 201  
 <211> 120  
 <212> PRT  
 <213> Homo sapien

<400> 201
Met Glu Thr Pro Ser Gln Arg Arg Ala Thr Arg Ser Gly Ala Gln Ala
1 5 10 15
Ser Ser Thr Pro Leu Ser Pro Thr Arg Ile Thr Arg Leu Gln Glu Lys
20 25 30
Glu Asp Leu Gln Glu Leu Asn Asp Arg Leu Ala Val Tyr Ile Asp Arg
35 40 45
Val Arg Ser Leu Glu Thr Glu Asn Ala Gly Leu Arg Leu Arg Ile Thr
50 55 60
Glu Ser Glu Glu Val Val Ser Arg Glu Val Ser Gly Ile Lys Ala Ala
65 70 75
Tyr Glu Ala Glu Leu Gly Asp Ala Arg Lys Thr Leu Asp Ser Val Ala
85 90 95
Lys Glu Arg Ala Arg Leu Gln Leu Glu Leu Ser Lys Val Arg Glu Glu
100 105 110
Phe Lys Glu Leu Lys Ala Arg Asn
115 120

<210> 202  
 <211> 177  
 <212> PRT  
 <213> Homo sapien

<400> 202
Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile
1 5 10 15
Lys Met Glu Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly
20 25 30
Ala Pro Gly Pro Lys Gly Glu Gly Glu Arg Pro Ala Gln Asn Glu Lys
35 40 45
Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr
50 55 60
Ala Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe
65 70 75
Asp Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly
85 90 95
Glu Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg
100 105 110
Gly Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala
115 120 125
Ala Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val

130                      135                      140  
 Lys Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala  
 145                      150                      155                      160  
 Gly Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val  
                     165                      170                      175  
 Gly

<210> 203  
 <211> 164  
 <212> PRT  
 <213> Homo sapien

<400> 203  
 Met Arg Leu Ala Val Gly Ala Leu Leu Val Cys Ala Val Leu Gly Leu  
 1                      5                      10                      15  
 Cys Leu Ala Val Pro Asp Lys Thr Val Arg Trp Cys Ala Val Ser Glu  
                     20                      25                      30  
 His Glu Ala Thr Lys Cys Gln Ser Phe Arg Asp His Met Lys Ser Val  
                     35                      40                      45  
 Ile Pro Ser Asp Gly Pro Ser Val Ala Cys Val Lys Lys Ala Ser Tyr  
 50                      55                      60  
 Leu Asp Cys Ile Arg Ala Ile Ala Ala Asn Glu Ala Asp Ala Val Thr  
 65                      70                      75  
 Leu Asp Ala Gly Leu Val Tyr Asp Ala Tyr Leu Ala Pro Asn Asn Leu  
                     85                      90                      95  
 Lys Pro Val Val Ala Glu Phe Tyr Gly Ser Lys Glu Asp Pro Gln Thr  
                     100                      105                      110  
 Phe Tyr Tyr Ala Val Ala Val Val Lys Lys Asp Ser Gly Phe Gln Met  
                     115                      120                      125  
 Asn Gln Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser  
 130                      135                      140  
 Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro Glu  
 145                      150                      155                      160  
 Pro Arg Lys Pro

<210> 204  
 <211> 241  
 <212> PRT  
 <213> Homo sapien

<400> 204  
 Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro  
 1                      5                      10                      15  
 Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys  
                     20                      25                      30  
 Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg  
                     35                      40                      45  
 His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe  
 50                      55                      60  
 Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly  
 65                      70                      75  
 Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala  
                     85                      90                      95  
 Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys  
                     100                      105                      110  
 Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly

[illegible]

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<210> 205
<211> 160
<212> PRT
<213> Homo sapien
```

<400> 205																	
Met	Gln	Ile	Phe	Val	Lys	Thr	Leu	Thr	Gly	Lys	Thr	Ile	Thr	Leu	Glu		
1				5					10					15			
Val	Glu	Pro	Ser	Asp	Thr	Ile	Glu	Asn	Val	Lys	Ala	Lys	Ile	Gln	Asp		
				20				25					30				
Lys	Glu	Gly	Ile	Pro	Pro	Asp	Gln	Gln	Arg	Leu	Ile	Phe	Ala	Gly	Lys		
		35					40				45						
Gln	Leu	Glu	Asp	Gly	Arg	Thr	Leu	Ser	Asp	Tyr	Asn	Ile	Gln	Lys	Glu		
	50					55					60						
Ser	Thr	Leu	His	Leu	Val	Leu	Arg	Leu	Arg	Gly	Gly	Met	Gln	Ile	Phe		
65				70						75					80		
Val	Lys	Thr	Leu	Thr	Gly	Lys	Thr	Ile	Thr	Leu	Glu	Val	Glu	Pro	Ser		
				85					90					95			
Asp	Thr	Ile	Glu	Asn	Val	Lys	Ala	Lys	Ile	Gln	Asp	Lys	Glu	Gly	Ile		
			100					105					110				
Pro	Pro	Asp	Gln	Gln	Arg	Leu	Ile	Phe	Ala	Gly	Lys	Gln	Leu	Glu	Asp		
		115				120						125					
Gly	Arg	Thr	Leu	Ser	Asp	Tyr	Asn	Ile	Gln	Lys	Glu	Ser	Thr	Leu	His		
	130					135					140						
Leu	Val	Leu	Arg	Leu	Arg	Gly	Gly	Met	Gln	Ile	Phe	Val	Lys	Thr	Leu		
145				150						155					160		

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<210> 206
<211> 197
<212> PRT
<213> Homo sapien
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<400> 206																	
Thr	Ser	Pro	Ser	Glu	Ala	Cys	Ala	Pro	Leu	Ile	Ser	Leu	Ser	Thr			
1				5					10				15				
Leu	Ile	Tyr	Asn	Gly	Ala	Leu	Pro	Cys	Gln	Cys	Asn	Pro	Gln	Gly	Ser		
			20					25					30				
Leu	Ser	Ser	Glu	Cys	Asn	Pro	His	Gly	Gly	Gln	Cys	Leu	Cys	Lys	Pro		
			35				40					45					
Gly	Val	Val	Gly	Arg	Arg	Cys	Asp	Leu	Cys	Ala	Pro	Gly	Tyr	Tyr	Gly		

50                      55                      60  
 Phe Gly Pro Thr Gly Cys Gln Gly Ala Cys Leu Gly Cys Arg Asp His  
 65                      70                      75                      80  
 Thr Gly Gly Glu His Cys Glu Arg Cys Ile Ala Gly Phe His Gly Asp  
                     85                      90                      95  
 Pro Arg Leu Pro Tyr Gly Gly Gln Cys Arg Pro Cys Pro Cys Pro Glu  
                     100                      105                      110  
 Gly Pro Gly Ser Gln Arg His Phe Ala Thr Ser Cys His Gln Asp Glu  
                     115                      120                      125  
 Tyr Ser Gln Gln Ile Val Cys His Cys Arg Ala Gly Tyr Thr Gly Leu  
 130                      135                      140  
 Arg Cys Glu Ala Cys Ala Pro Gly His Phe Gly Asp Pro Ser Arg Pro  
 145                      150                      155                      160  
 Gly Gly Arg Cys Gln Leu Cys Glu Cys Ser Gly Asn Ile Asp Pro Met  
                     165                      170                      175  
 Asp Pro Asp Ala Cys Asp Pro His Thr Gly Gln Cys Leu Arg Cys Leu  
                     180                      185                      190  
 His His Thr Glu Gly  
                     195

&lt;210&gt; 207

&lt;211&gt; 175

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 207

Ile Ile Arg Gln Gln Gly Leu Ala Ser Tyr Asp Tyr Val Arg Arg Arg  
 1                      5                      10                      15  
 Leu Thr Ala Glu Asp Leu Phe Glu Ala Arg Ile Ile Ser Leu Glu Thr  
                     20                      25                      30  
 Tyr Asn Leu Leu Arg Glu Gly Thr Arg Ser Leu Arg Glu Ala Leu Glu  
                     35                      40                      45  
 Ala Glu Ser Ala Trp Cys Tyr Leu Tyr Gly Thr Gly Ser Val Ala Gly  
 50                      55                      60  
 Val Tyr Leu Pro Gly Ser Arg Gln Thr Leu Ser Ile Tyr Gln Ala Leu  
 65                      70                      75                      80  
 Lys Lys Gly Leu Leu Ser Ala Glu Val Ala Arg Leu Leu Leu Glu Ala  
                     85                      90                      95  
 Gln Ala Ala Thr Gly Phe Leu Leu Asp Pro Val Lys Gly Glu Arg Leu  
                     100                      105                      110  
 Thr Val Asp Glu Ala Val Arg Lys Gly Leu Val Gly Pro Glu Leu His  
                     115                      120                      125  
 Asp Arg Leu Leu Ser Ala Glu Arg Ala Val Thr Gly Tyr Arg Asp Pro  
 130                      135                      140  
 Tyr Thr Glu Gln Thr Ile Ser Leu Phe Gln Ala Met Lys Lys Glu Leu  
 145                      150                      155                      160  
 Ile Pro Thr Glu Glu Ala Leu Arg Leu Trp Met Pro Ser Trp Pro  
                     165                      170                      175

&lt;210&gt; 208

&lt;211&gt; 177

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 208

Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile  
 1                      5                      10                      15  
 Lys Met Glu Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly

[illegible]

```
<210> 209
<211> 196
<212> PRT
<213> Homo sapien
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[illegible]

<210>	210
<211>	156
<212>	PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 210

```

Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly Lys Glu
 1          5          10          15
Val Leu Leu Leu Ala His Asn Leu Pro Gln Asn Arg Ile Gly Tyr Ser
 20          25          30
Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Ser Leu Ile Val Gly Tyr
 35          40          45
Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser Gly Arg
 50          55          60
Glu Thr Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Val Thr Gln
 65          70          75          80
Asn Asp Thr Gly Phe Tyr Thr Leu Gln Val Ile Lys Ser Asp Leu Val
 85          90          95
Asn Glu Glu Ala Thr Gly Gln Phe His Val Tyr Pro Glu Leu Pro Lys
100          105          110
Pro Ser Ile Ser Ser Asn Asn Ser Asn Pro Val Glu Asp Lys Asp Ala
115          120          125
Val Ala Phe Thr Cys Glu Pro Glu Val Gln Asn Thr Thr Tyr Leu Trp
130          135          140
Trp Val Asn Gly Gln Ser Leu Pro Val Ser Pro Lys
145          150          155

```

&lt;210&gt; 211

&lt;211&gt; 92

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 211

```

Met Glu Ser Pro Ser Ala Pro Pro His Arg Trp Cys Ile Pro Trp Gln
 1          5          10          15
Arg Leu Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr
 20          25          30
Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly
 35          40          45
Lys Glu Val Leu Leu Leu Val His Asn Leu Pro Gln His Leu Phe Gly
 50          55          60
Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Arg Gln Ile Ile
 65          70          75          80
Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly
 85          90

```

&lt;210&gt; 212

&lt;211&gt; 142

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 212

```

Glu Lys Gln Lys Asn Lys Glu Phe Ser Gln Thr Leu Glu Asn Glu Lys
 1          5          10          15
Asn Thr Leu Leu Ser Gln Ile Ser Thr Lys Asp Gly Glu Leu Lys Met
 20          25          30
Leu Gln Glu Glu Val Thr Lys Met Asn Leu Leu Asn Gln Gln Ile Gln
 35          40          45
Glu Glu Leu Ser Arg Val Thr Lys Leu Lys Glu Thr Ala Glu Glu Glu
 50          55          60
Lys Asp Asp Leu Glu Glu Arg Leu Met Asn Gln Leu Ala Glu Leu Asn

```

65	70								75				80			
Gly	Ser	Ile	Gly	Asn	Tyr	Cys	Gln	Asp	Val	Thr	Asp	Ala	Gln	Ile	Lys	
				85					90					95		
Asn	Glu	Leu	Leu	Glu	Ser	Glu	Met	Lys	Asn	Leu	Lys	Lys	Cys	Val	Ser	
			100					105					110			
Glu	Leu	Glu	Glu	Glu	Lys	Gln	Gln	Leu	Val	Lys	Glu	Lys	Thr	Lys	Val	
			115				120					125				
Glu	Ser	Glu	Ile	Arg	Lys	Glu	Tyr	Leu	Glu	Lys	Ile	Gln	Gly			
	130					135				140						

```
<210> 213
<211> 142
<212> PRT
<213> Homo sapien
```

<400> 213																	
Gly	Gly	Tyr		Gly	Gly	Gly	Tyr	Gly	Gly	Val	10	Leu	Thr	Ala	Ser	Asp	Gly
1				5												15	
Leu	Leu	Ala	Gly	Asn	Glu	Lys	Leu	Thr	Met	Gln	Asn	Leu	Asn	Asp	Arg		
			20						25						30		
Leu	Ala	Ser	Tyr	Leu	Asp	Lys	Val	Arg	Ala	Leu	Glu	Ala	Ala	Asn	Gly		
		35					40						45				
Glu	Leu	Glu	Val	Lys	Ile	Arg	Asp	Trp	Tyr	Gln	Lys	Gln	Gly	Pro	Gly		
		50				55					60						
Pro	Ser	Arg	Asp	Tyr	Ser	His	Tyr	Tyr	Thr	Thr	Ile	Gln	Asp	Leu	Arg		
65				70						75					80		
Asp	Lys	Ile	Leu	Gly	Ala	Thr	Ile	Glu	Asn	Ser	Arg	Ile	Val	Leu	Gln		
				85					90						95		
Ile	Asp	Asn	Ala	Arg	Leu	Ala	Ala	Asp	Asp	Phe	Arg	Thr	Lys	Phe	Glu		
			100					105					110				
Thr	Glu	Gln	Ala	Leu	Arg	Met	Ser	Val	Glu	Ala	Asp	Ile	Asn	Gly	Leu		
		115					120					125					
Arg	Arg	Val	Leu	Asp	Glu	Leu	Thr	Leu	Ala	Arg	Thr	Asp	Leu				
		130				135					140						

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<210> 214
<211> 129
<212> PRT
<213> Homo sapien
```

[illegible]



<210> 215  
 <211> 148  
 <212> PRT  
 <213> Homo sapien

<400> 215  
 Met Ala Thr Leu Lys Glu Lys Leu Ile Ala Pro Val Ala Glu Glu Glu  
 1 5 10 15  
 Ala Thr Val Pro Asn Asn Lys Ile Thr Val Val Gly Val Gly Gln Val  
 20 25 30  
 Gly Met Ala Cys Ala Ile Ser Ile Leu Gly Lys Ser Leu Ala Asp Glu  
 35 40 45  
 Leu Ala Leu Val Asp Val Leu Glu Asp Lys Leu Lys Gly Glu Met Met  
 50 55 60  
 Asp Leu Gln His Gly Ser Leu Phe Leu Gln Thr Pro Lys Ile Val Ala  
 65 70 75 80  
 Asp Lys Asp Tyr Ser Val Thr Ala Asn Ser Lys Ile Val Val Val Thr  
 85 90 95  
 Ala Gly Val Arg Gln Gln Glu Gly Glu Ser Arg Leu Asn Leu Val Gln  
 100 105 110  
 Arg Asn Val Asn Val Phe Lys Phe Ile Ile Pro Gln Ile Val Lys Tyr  
 115 120 125  
 Ser Pro Asp Cys Ile Ile Ile Val Val Ser Asn Pro Val Asp Ile Leu  
 130 135 140  
 Thr Tyr Val Thr  
 145

<210> 216  
 <211> 527  
 <212> PRT  
 <213> Homo sapien

<400> 216  
 Gln Arg Ala Pro Gly Ile Glu Glu Lys Ala Ala Glu Asn Gly Ala Leu  
 1 5 10 15  
 Gly Ser Pro Glu Arg Glu Glu Lys Val Leu Glu Asn Gly Glu Leu Thr  
 20 25 30  
 Pro Pro Arg Arg Glu Glu Lys Ala Leu Glu Asn Gly Glu Leu Arg Ser  
 35 40 45  
 Pro Glu Ala Gly Glu Lys Val Leu Val Asn Gly Gly Leu Thr Pro Pro  
 50 55 60  
 Lys Ser Glu Asp Lys Val Ser Glu Asn Gly Gly Leu Arg Phe Pro Arg  
 65 70 75 80  
 Asn Thr Glu Arg Pro Pro Glu Thr Gly Pro Trp Arg Ala Pro Gly Pro  
 85 90 95  
 Trp Glu Lys Thr Pro Glu Ser Trp Gly Pro Ala Pro Thr Ile Gly Glu  
 100 105 110  
 Pro Ala Pro Glu Thr Ser Leu Glu Arg Ala Pro Ala Pro Ser Ala Val  
 115 120 125  
 Val Ser Ser Arg Asn Gly Gly Glu Thr Ala Pro Gly Pro Leu Gly Pro  
 130 135 140  
 Ala Pro Lys Asn Gly Thr Leu Glu Pro Gly Thr Glu Arg Arg Ala Pro  
 145 150 155 160  
 Glu Thr Gly Gly Ala Pro Arg Ala Pro Gly Ala Gly Arg Leu Asp Leu  
 165 170 175  
 Gly Ser Gly Gly Arg Ala Pro Val Gly Thr Gly Thr Ala Pro Gly Gly



<210> 218  
 <211> 381  
 <212> DNA  
 <213> Homo sapien

<400> 218  
 gagtttcctt cgcaagtcca tgtgggggtac cttccaggcg tgccctggctg accagctgggt 60  
 tttaaagcgc cggggtaaac agttggagat ctgtgcccgtg gtcctgaggc agttgtctcc 120  
 acacaagtac tacttccctcg tgggctacag tgaaactttg ctgtcctact tttaacaaatg 180  
 tccctgtcgca ctccacctcc aaactgtgcc ctcaaaagtt gtgtataagt acctctagaa 240  
 caatccccctt ttttccatca agctgtagcc tgcagagaat ggaacacgtg gaaggaatg 300  
 gtatgtgggg gaaatgcac cctcagagg actgaggcat agtctctcat ctgctattga 360  
 ataaagacct tctatcttgt a 381

<210> 219  
 <211> 1293  
 <212> DNA  
 <213> Homo sapien

<400> 219  
 gaggggaggg ccatggcggt gatggcgctg ggcggggcct ggaagcagat gtcctgggttc 60  
 tactaccagt acctgctggt caccggcgctc tacatgctgg agccctggga ggcgacgggtg 120  
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<210> 220  
 <211> 983  
 <212> DNA  
 <213> Homo sapien

<400> 220  
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 tcaactgtagt tactttccct cgagtgccca aatgcccaat aagaaggaat accatgaccac 180  
 tgctgtgggg agtcagcagg tgcgtgatgc agctggccac actccatcca cgcctgtgac 240  
 ataaaaaga caagaagtaa ggctggactg taacacotca aggcctgtcc cagtacccca 300  
 cttttctcag agaggtccta ccacacacac aaccaccttc caaatttaca ctcatgacac 360  
 tacaccatgt ctcccaagtt aaaacatgta tccacctaga ctttaaatgt gctttgtaac 420  
 tgttgatggc actgtacaga gggccaaagt atttcccatc agatagcatt tttctgaacc 480

catgcctctt	gggacgagat	cacaggactt	gaacctcat	caaataggac	caggtgacct	540
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gagacaatta	taaaacttgat	agattttgat	gtgtgaagggt	atttatgaat	atttttagtc	720
agtgtggta	tactgttaag	gaaaagggtc	atatttttag	gacaaaggct	gaaacatttta	780
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aaaaaaaaa	aaaaaaactc	gag				983

&lt;210&gt; 221

&lt;211&gt; 373

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 221

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ataaggggaa	aatacaataa	tgttgagaaa	gcaaaactcaa	agcatagatc	aatgaaaaaa	240
ttgagaaatg	gacataaatg	atttagtatt	tttaaagaga	gtgaaaaatc	attattttat	300
gcttttgtgt	agcggttagat	gaattaaata	acatatgcac	atatagcttt	gcgatacaaa	360
tttcagacc	ata					373

&lt;210&gt; 222

&lt;211&gt; 544

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 222

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ggaacataat	gtatttcaaa	acaaaataca	tgctcagttat	caagagactc	aacagatgca	180
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gttgaaaggt	caactacaag	aagctgagag	aaggtgggaa	gaagttcaga	gctacatcag	480
gaagagaaca	gcggaaacatg	aggcagcaca	gctagattta	cagagtaaat	ttgtggccaa	540
agaa						544

&lt;210&gt; 223

&lt;211&gt; 316

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 223

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atatcttggt	ttcttctaca	ccaataaatg	aaggacagac	tggtgttagac	aaggtggctg	240
agcagtgta	acctgctgaa	agtcagccag	aagcacttct	gagaggaaga	tgtttgcaag	300
gtaactctaa	cagttg					316

&lt;210&gt; 224

&lt;211&gt; 1583

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 224

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cacagaagaa	aagctgtggcc	aggctgagaa	gacagaattg	gatgctcact	tagaagaacct	240
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aaaagctcca	agtcgtataa	acaaccagaa	acttttggga	caatatatga	ttgatgcagg	420
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tttttcatta	acagcaagct	ttttttttta	tgtaaaaata	atctattgtg	aattgaaaaa	1560
aaaaaaaaaa	aaaaaaactc	gag				1583

&lt;210&gt; 225

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 225

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acaatcaagg	ttaggcaact	agattcagca	ttggaaattt	gtaaggaaga	actgtctgtg	180
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gaagaggat	attgtttaca	gaaagagcta	aagataaaaa	atcacagtct	tcaagagact	300
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gagacaatta	gaattggaga	gctagaagat	actcaaaact	aacttgaaaa	acaggtgtca	420
aaactggaac	aagaacttca	aaaacaagg	gaaagttcag	ctgaaaagtt	gagaaaaatg	480
gaggagaat	g					491

&lt;210&gt; 226

&lt;211&gt; 483

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 226

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aatgagtgta	agattttacag	cctcagctgc	ggcaagtcgc	ttcctgagtg	gctttctgat	180
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 <211> 486  
 <212> DNA  
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gcgacggcgg	cgacagcagg	tggccagcat	cgaaatgttc	agccttttag	tgatgaagat	180
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gatttaattg	acctaacctt	ggataagagt	gcgaagacaa	ggcaagcagc	tcttgaaggt	360
attaaaaatg	cactgtgcttc	aaaaatgctg	tatgaattta	ttctggaaag	gagaatgact	420
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gcagcg						486

<210> 228  
 <211> 494  
 <212> DNA  
 <213> Homo sapien

<400> 228						
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agaaaattgc	agaaagaaga	cttgctgttc	ttaagaggcc	cagggaaggtg	ctacttagga	420
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<210> 229  
 <211> 465  
 <212> DNA  
 <213> Homo sapien

<400> 229						
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gcagcggatc	cttttctctga	ccctcctaaa	ggcggttgccc	tcctatcctc	ccttctcttg	360
ccacccttgg	tttctttggc	atgggaaggt	tttctttaa	cacttgccct	agagccacca	420
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<210> 230  
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 <212> DNA  
 <213> Homo sapien

<400> 230						
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ccaaccaagt	gggtgtgaatt	ccaaaaacc	gtgggggtga	agggtctctt	aagaatgcaa	420
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<210> 231  
 <211> 498  
 <212> DNA  
 <213> Homo sapien

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<210> 232  
 <211> 465  
 <212> DNA  
 <213> Homo sapien

<400> 232						
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<210> 233  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(366)  
 <223> n = A,T,C or G

<400> 233						
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aatcacaaaa	aaatatacac	taacttataa	acaaaaagat	tatagtga	taaaatgta	180
tattctcttt	ttaagtggtg	aaaagtattt	tggtttgcttc	tacataaatt	tctattcatg	240
ananaataac	aaatattaaa	atacagtgat	agtttgcat	ttctctatag	aatgaacata	300
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ttatca						366

<210> 234  
 <211> 379  
 <212> DNA  
 <213> Homo sapien

<400> 234  
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 gaggagctgc aaaaactctc agggatgctg gtctggcagt cacagatgct tctgagttga 240  
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 <211> 406  
 <212> DNA  
 <213> Homo sapien

<400> 235  
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 gtttcagatt taattgtttt tgaccttcta aatgtttttt atgttagcac tgatagttgg 180  
 cattactggt gttaagcaact gtgttccaga ccgtgtctga cttagtgtaa cctaggagat 240  
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 tttacctgtc accgaagcca ggaagccccc tttgtaagcg tgtgtttgtg tgctttattg 360  
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<210> 236  
 <211> 278  
 <212> DNA  
 <213> Homo sapien

<400> 236  
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 caatggacag atactggaaa ccattggagg caaacaactc cgagttctttg tgtatcggac 180  
 ggctatctgc atagaaaaat catgcatggt gagaggaagc aagcaggga ggaacgggtgc 240  
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<210> 237  
 <211> 322  
 <212> DNA  
 <213> Homo sapien

<400> 237  
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 ccgcaacac ctactcctac ct 322

<210> 238  
 <211> 613  
 <212> DNA



<213> Homo sapiens

<220>

<221> misc feature

<222> (399)

<223> n=A,T,C or G

<400> 238

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ggtcccgctg ctg

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<210> 239

<211> 613

<212> DNA

<213> Homo sapiens

<400> 239

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gaattcgcca ccaggggaca ctgggtgctga gctggatgat gatcagcact ggtctgacag 60
cccgctggat gctgacagag agctgcgttt gccgtgccca gctgaggggg aagcagagct 120
ggagctgagg gtgtcggaag atgaggagaa gctgcccgc tcaccgaagc accaagagag 180
aggctccctc caagccacca gcccatcog gtctcccag gaatcagctc ttctgttcat 240
tcagtcacac agcccctcaa cagaggggcc ccaactccca cctgtccctg ccgccaccca 300
ggagaaatca cctgaggagc gccctttccc tgagcctttg ctcccaaaag agaagcccaa 360
agctgatgcc cctcggtatc tgaagctgt gcactctccc atccgatcac agccagtgc 420
cctgccagaa gctaggactc ctgtctcacc agggagcccg cagcccccag caccogtggc 480
ggcctccacg ccccaccda gcgaggtctc cagagccttc tctctcctg gcaaaatggc 540
aactcttaag gaaaaactca ttgcaccagt tgcggaagaa gaggcaacag ttccaaacaa 600
taagtactat gta

```

<210> 240

<211> 585

<212> DNA

<213> Homo sapiens

<400> 240

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gaattcgcca cgaggtgaga ttacgatga actttaagat tggaggtgtg acagaacgca 60
tgccaacccc agttatataa gcttttgcca tcttgaagcg agcgcccgct gaagtaaac 120
aggattatgg tcttgatcca aagattgcta atgcaataat gaaggcagca gatgagtag 180
ctgaaggttaa attaaatgat ctttttctc tcgtggtatg gcagactgga tcaggaaact 240
agacaaatct gaatgtaaat gaagtcatta gcaatagagc aattgaaatg ttaggaggtg 300
aacttggcag caagatacct gtgcaccca acgatcatgt taataaaagc cagagctcaa 360
atgatacttt tcccacagca atgcacattg ctgctgcaat agaagttcat gaagtactgt 420
tcaccagact acagaagtta catgatgctc ttgatgcata atccaaagag tttgcacaga 480
tcatcaagat tggagctact catactcagg atgctgttcc acttactctt gggcaggagat 540
ttagtgggta tgttcaacaa gtaaaaatat caatgacaa aataa

```

<210> 241

<211> 566

<212> DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 241

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gaattcgcca ccaggcgagc tgcacctga ggtgaagcc tcaactgatga acgatgactt 60
cgagaagatc agaaactggc agaaggaagc ctttcacaag cagatgatgg gcggtctcaa 120
ggagaccaag gaagctgagg acggcttttc gaaggcacag aagccctggg ccaagaagct 180
gaaagaggtga gaagcagcaa agaaagccca ccatgcagcg tgcaaaagagg agaagctggc 240
tatctcacga gaagccaaca gcaaggcaga cccatccctc aacctgaac agctcaagaa 300
attgcaagac aaaaatagaaa agtgcaggca agatgttctt aagaccaaaag agaagtatga 360
gaagtccttg aaggaaactcg accagggcac accccagtac atggagaaaca tggagcaggt 420
gitttgacag tgcacagcagt tcgaggagaa acgccttcgc ttcttcgggg aggtttctgct 480
ggagggtttag aagcacctag acctgtgcaa tgtggctggc tacaagacca ttaccatga 540
cctggagcag agcatcagag cagctg

```

&lt;210&gt; 242

&lt;211&gt; 556

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 242

```

gaattcgcca cgagcaaaagg tgaagcagga catgcctcgg cccgggggct atgggcccac 60
cgactacaaa cggaaactgc cgcgtcgagg actgtcgggc tacagcatgc tggccatagg 120
gattggaacc ctgatctacg ggcactggag cataatgaag tggaaacctg agcgcaggcg 180
cctacaaatc gaggacttcg aggtcgcgat cgcgtgttgg ccaactgttac aggcagaaac 240
cgaccggagg accttgcaga tgcttcggga gaacctggag gaggaggcca tcatcatgaa 300
ggacgtgccc gacttgaagg tgggggagtc tgtgttccac acaaccgcgt ggggtgcccc 360
cttgatcggg gagctgcagc ggctgcgcac cacagaggag gctctccatg ccagccacgg 420
cttcatgtgg tacacgtagg cctgtgccc tcgggccacc tggatccctg cccctcccca 480
ctgggacgga ataaatgctc tgcagacctg gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540
aaaaaaaaaa ctcgag

```

&lt;210&gt; 243

&lt;211&gt; 591

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 243

```

gtctatgttt gcgaaatcac agatccaaga caaagacagg atgggcactg ctggaaaaagt 60
tattaaatgc aaagcagctg tgctttggga gcagaagcaa ccttctccca ttgaggaaat 120
agaagtgtcc ccaccaaaga ctaaagaagt tcgcattaag attttggcca caggaaatctg 180
tcgcacagat gaccatgtga taaaaggaaac aatggtgtcc aagtttccag tgatttgtgtg 240
acatgagcca actgggattg tagagagcat tggagaagga gtgactacag tgaaccagg 300
tgacaaagtc atccctctct ttctgccaca atgtagagaa tgcaatgctt gtcgcaaccc 360
agatggcaac ctttgcatta ggagcgatat tactggtcgt ggagtactgg ctgatggcac 420
caccagattt acatgcaagg gcaaacaggt ccaccacttc atgaacacca gtacatttac 480
cgagtacaca gtggtggagt aatcttctgt tgctaagatt gatgatgcag ctccctcctga 540
gaaagtctgt taaattggct gtgggttttc cctggatat ggcgtgctg t

```

&lt;210&gt; 244

&lt;211&gt; 594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 244

```

gaattcgcca cgagaacaga gtgaactgag catcagtcag aaaaagtcta tgtttgcaga 60
aatacacatc caagacaaag acaggatggg cactgctgga aagttatta aatgcaaggc 120
agctgtgctt tgggagcaga agcaaccctt ctccattgag gaaatagaag ttgccccacc 180
aaagactaaa gaagttcgca ttaagatttt ggccacagga atctgtcgca cagatgacca 240

```

```

tgtgataaaa ggaacaatgg tgtccaagtt tccagtgatt gtgggacatg aggcaactgg 300
gattgtagag agcattggag aaggagtgcac tacagtgaaa ccaggtgaca aagtcattccc 360
tctctttctg ccacaatgta gagaatgcaa tgcttgtcgc aaccagatg gcaacctttg 420
cattaggagc gatattactg gtctgtggagt actggctgat ggcaccacca gatttacatg 480
caagggcaaa ccagtcacc acttcatgaa caccagtaca tttaccgagt acacagtgg 540
ggatgaattc tctgttgcta agattgatga tgcagctcct cctgagaaaag tctg 594

```

&lt;210&gt; 245

&lt;211&gt; 615

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (105)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 245

```

gtccctttcc tctgtgcgc ctcggtcacg ctgtgtcccg aaggaggaaa cagtgcaga 60
cttgagagct gcagttctct atccttcac agctctttca ccatnctgga tcacttcctt 120
tgaatcgaga agcttgcctg ccaaagatg tgggaattgt tgcccttgag atctattttc 180
cttctcaata ttttgatcaa gcagagttgg aaaaatatga ttggttagat gctggaaaagt 240
ataccattgg ctgtggccag gccaaagatg gcttctgcac agatagagaa gatattaact 300
ctcttttgcat gactgtggtt cagaatctta tggagagaaa taacctttcc tatgattgca 360
ttgggcggct ggaagttgga acagagacaa tcacgcagaa atcaaagtct gtgaagacta 420
atttgatgca gctgtttgaa' gactctggga atacagatat agaaggaatc gacacacta 480
atgcattgcta tggaggcaca gctgctgtct tcaatgcttg ttaactggat tgagtcacag 540
tcttgggatg gacggtatgc cctggttaagt tgcaggagat attgctgtat atgccacagg 600
aaatgctaga cctac 615

```

&lt;210&gt; 246

&lt;211&gt; 546

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 246

```

gaattcgcca ccaggctgcc tcccgctcgc cctgaaccca gtgcctgcag ccatggetcc 60
cgccagagctc gccattattta gtgtctctgc aaaaccggcc ttgtgaattt gcaagaaacc 120
tgaccgctct tggtttgat ctgtctgcct ccggaggagc tgcaaaagct ctacgggatg 180
ctggtctggc agtcagagat gtctctgagt tgacgggatt tgcctgaaat ttggggggag 240
gtgtgaaaaa ttgtcatcct gcagtcocat ctggaatcct agctcgtaat atccagaaag 300
ataatgctga catggccaga cttgatttca atcttataag agttgttgc tgcaatctct 360
atccctttgt aaagacagtg gcttctccag gtgtaactgt tgaggaggct gtggagcaaa 420
ttgacattgg tggagtaacc ttactgagag ctgcagccaa aaaccacgct cgagtgcag 480
tggtgtgtga accagaggac tatgtgggtg ggtgtccacg gagatgcaga gctccgagag 540
taaggaa 546

```

&lt;210&gt; 247

&lt;211&gt; 564

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 247

```

gaattcgcca ccagagatca cgtgcagtga gatgcagcaa aaagttgaac ttctgagata 60
tgaatctgaa aagcttcaac aggaataatc tattttgaga aatgaaatta ctactttaaa 120
tgaagaagat agcatttcta acctgaaatt agggacatta aatggatctc aggaagaaat 180
gtgacaaaaa acggaaactg taaaacaaga aatgtctgca gttcagata ttggttgaaa 240
tttaaaagaa cagatttcag aattaaaaat caaaaaccaa caattggatt tggaaaatac 300

```

```

agaacttagc caaaagaact ctcaaaacca gaaaaaactg caagaactta atcaactgtc 360
aacagaaaat ctatgccaga aggaaaaaga gccagggaac agtgcatgtg aggaacggga 420
acaagagaag tttaatctga aagaagaact ggaacgttgt aaagtgcagt cctccacttt 480
agtgtcttct ctggaggcgg agctctctga agttaaataa cagaccataa ttgtgcaaca 540
ggaaaaccaac cttctcaagg atga

```

&lt;210&gt; 248

&lt;211&gt; 434

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 248

```

gttcttgttt gtggatcgct gtgatcgtaa cttgacaatg cagatcttcg tgaagactct 60
gactggttaag accatcaccc tcgaggttga gccagtgac accatcgaga atgtcaaggc 120
aaagatccaa gataagggaag gcatccctcc tgaccagcag aggtgatctt ttgctggaaa 180
acagctggaa gatgggcgca cctgtctga ctacaacatc cagaagaagt ccacctgtga 240
cctgtgtctc cgtctcaagg gtgggatgca aatcttctgt aagacactca ctggcaagac 300
catcaccctt gaggtggagc ccagtgacac catcgagaac gtcaaaagca agatccagga 360
caagggaagg atctctctcg accagcagag gttgatcttt gccggaaaag cagcctggga 420
agatggggcc gcc

```

&lt;210&gt; 249

&lt;211&gt; 416

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 249

```

gccccccagc gagggcgagg cgccggcgcc ggacggggcc cccgcggcag acggcgaggga 60
cggacaggac ccgcacagca agcacctgta cccggccgac atgttcaagc accggatcca 120
gagcgccgag cactctgtca tttctcttgc gccctgtgtg ggacactgcc acggcggtga 180
gccgactgtg aatgaactgg gagacaaata caacagcatg gaagatgccaa aagtctatgt 240
ggctaagtgt gactgcacgg ccactccgga cgtgtgtctc gccacggggg tgcgaggata 300
cccacactta agctctttca agccaggcca agaagctgtg aagtaccagg gtccctcgga 360
cttcagaca ctgaaaaact ggatgctgca gacactgaac gaggagccag tgacac 416

```

&lt;210&gt; 250

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 250

```

gaattcgcca cgaggcgagg aacgttatag tatttgcagc aagtgggggt ctccgtgggc 60
attgtgatcc gtcccaggca gtgattatag agggccagaag gagatccctt ccacgggtgct 120
aggctgagat ggatcctctc agggcccaac agctggctgc ggagctggag ttggagatga 180
tgccgatgat gtacaaacaga atgaccagtg cctgccaccg gaagtgtgtg cctcctcact 240
acaagggaagc agaactctcc aaggcgagtg ctgtgtgtct ggacagatgt gtctctaagt 300
acctggacat ccatgagcgg atgggcaaaa agttgacaga gttgtctatg caggatgaag 360
agctgatgaa gaggtgtcag cagagctctg ggctgcatg aggtccctgt cagtatacac 420
cctgggggtg acccccacc cttccacttt aataaacgtg ctccctgttg ggtgtcatct 480
gtgaagactg ccaggcctag ctct

```

&lt;210&gt; 251

&lt;211&gt; 607

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 251

```

gatgaaataa cacaatttta ctgacaaatg cctctactgt aatcgctatt taccacaga 60

```

tactctgtctc	aacctatgt	taattcatgg	tctgtctgt	ccatattgcc	gttcaacttt	120
caatgatgtg	gaaaagatgg	ccgcacacat	gcgatgggt	cacattgatg	aagagatggg	180
acctaaaaca	gattctactt	tgagttttga	tttgacattg	cagcagggtg	gtcacactaa	240
catccatctc	ctggtaacta	catacaatct	gagggatgcc	ccagctgaat	ctgttgctta	300
ccatgcccaa	aataatctct	cagttcctcc	aaagccacag	ccaaaggttc	agggaaaagg	360
agatatccct	gtaaaaagtt	cacctcaagc	tcagtgccc	tataaaaaag	atgttgggaa	420
aacctttgtg	ctcttttgct	tttcaatcct	aaaaggaccc	atatctgatg	cacttgccaa	480
tacttaagc	gagagggtcc	aagtatttca	gcaggttcac	ccagttgaga	aaaagctcac	540
ctcaaatgt	atccattgcc	ttggtgtgta	taccagcaac	atgaccgcct	caactatcac	600
ctcgcat						607

&lt;210&gt; 252

&lt;211&gt; 618

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 252

gaattgcac	cagggggtcct	gctggtcttc	gcctttcttc	tccgcttcta	ccccgtgggc	60
cgctgccact	gggggtccctg	gccccacoga	catggcgcg	gtgttgagca	agtcctggag	120
cgacgggagc	tgaacaagct	gcccagaagt	gtccagaaca	aacttgaaa	gttctgtgt	180
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gaacaacagt	attttgaat	agaaaagagg	ttgtcccaca	gtcaggagag	actctgtgaat	300
gaaacccgag	agtgtcaaa	cttgcggctt	gagctagaga	aactcaacaa	tcaactgaag	360
gcactaactg	agaaaaacaa	agaacttgaa	atgctcagg	atcgcaatat	tgccattcag	420
agccaattta	caagaacaaa	ggaagaatta	gaagctgaga	aaagagactt	aattagaacc	480
aatgagagac	tatctcaaga	acttgaatac	ttacagagg	atgttaaacg	tctgaatgaa	540
aaacttaaa	aaagcaatc	aaacaaaggt	gaacttcagt	taaaattgga	tgaacttcaa	600
gctctgatg	tttctgtt					618

&lt;210&gt; 253

&lt;211&gt; 1201

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 253

gaattgcgca	ccaggggtggc	gagcgcggt	gctgtgctg	ggcgagcagc	ggggaccgtg	60
tgtgattgtg	gcgatgtttg	gtccccctgg	attctgcctt	agcaagaaga	aagtgtgaaa	120
tacttctctg	aagaaaaacta	aaacaataca	aaagccacag	cttattgatt	gcattgtcag	180
ccctttacaa	atatggcacac	atttctctagc	ctatttccac	ctggaggaga	tagtaggctg	240
aatcctgagc	ctgagttcca	aaatatgtta	atgatgaaa	gggtacgctg	tgaacatcat	300
aaacataatt	atcaggctct	gaaaattgaa	cacaaaaggt	tgcaggaaga	atatgtaaaa	360
tcacaaaatg	aacttaaaag	tgtattaatt	gaaaagcaag	caagccagga	aaaattccaa	420
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gctgagtata	acaaagctgc	ctacagat	acatttctca	agtcagagtt	tgaacaccag	660
aaagaagaag	ttactcgggt	ttcagaagaa	gagaaaatga	aatacaagtc	agaggttgca	720
cgactggaga	agggacaaaga	ggagctacat	aaccagctgc	ttagtgttga	tcccacgaga	780
gacagcaaac	gaatggagca	acttgttcga	gaaaaaaccc	atttgcctca	gaaattgaaa	840
agtttagagc	ctgaagtga	agaattaaag	ctgtgagaag	aaaattctgt	tgctcaggtg	900
gaaaatgtcc	aaaagataca	ggtgaggcag	ttggctgaga	tgcaggtcac	actcagatcc	960
ttggaggctg	aaaagcagtc	agctaaacta	caagctgagc	gttttagaaa	agaactacaa	1020
tcagacaaat	acagagaatc	ctgcttaatc	agcaaacctg	atagagctga	ccgagaatc	1080
agcacactgg	ccagtgaatg	gaaagagctt	aaacatgcaa	acaaactgca	ataagctgac	1140
atcaaacctg	aggcagcaag	agctaagagt	gagctcgaaa	gagaaaggaa	taagatccaa	1200
a						1201

&lt;210&gt; 254

<211> 560  
 <212> DNA  
 <213> Homo sapiens

<400> 254  
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 ctgatgtttt tgcagattac ctccaggaaa cggaggtttg ttgagttaca gacacattaa 120  
 accaaaggcc gtgggaaaac ccctctccag ctccagggga ttggtcagga ccaccacta 180  
 accagtgctt tcctctctaa cattcacttt tagcagcttg tgtttatatt acatggggcag 240  
 ttttgatggg aaattgccat gaccacaggg gtttggagtt ctgctttttt tttttctctt 300  
 tctttttcgg gggactgggg gactcctccc aagatcacat tttagcatct ttctctccta 360  
 ctccatttag aaaaaataag aacaggtgaa atgtggtctc agtgtaaacg ggataattct 420  
 gctaccggct cctcctgat gattctgaaa tacactactg aacgagctct ggctggctct 480  
 ttctatctgt gatgtgggtc ttctgtgtag caattccttg atgtccagtt tggaaagatg 540  
 tactctcttc aacaagaaaa

<210> 255  
 <211> 612  
 <212> DNA  
 <213> Homo sapiens

<400> 255  
 gaattcggca ccaggcgggg cagcaggggc ggggccatgg ggagcttgaa ggaggagctg 60  
 ctcaaaagcca tctggcacgc ctccaccgac tgcaccagga ccacagggca agtctctcaa 120  
 gtccagcttc aaggtccttt ccataacct gtgcacgggt ctgaaggctc ctcatgacct 180  
 agttgccttt gaagagcact tcagggatga tgatgagggt ccagtgcca accagggcta 240  
 catgccttat ttaaacaggt tcattttgga aaaggtccaa gacaactttg acaagattga 300  
 attcaatagg atgtgttgga cctctgtgtt caaaaaaaa cctcacaaag aatccctctg 360  
 tcattacaga agaagatgca tttaaaatat ggggtatttt caacttttta tctgaggaca 420  
 agtatccatt aattattgtg tcagaagaga ttgaatacct gcttaagaag cttaacagaag 480  
 ctatgggagg aggttgccag caagaacaat ttgaacatta taaaatcaac ttgatgaca 540  
 gtaaaaatgg cctttctgca tgggaactta ttgagcttat tggaaatgga cagtttagca 600  
 aaggcatgga cc

<210> 256  
 <211> 1132  
 <212> DNA  
 <213> Homo sapiens

<400> 256  
 gaattcggca cgaggtctgg gagaggcctc tggagcagga ggccagctgg ctcttctgac 60  
 ccaggccccc gcgctccagc ttctaagtcg cagatgatgg aggagcgtgc caacctgatg 120  
 cacatgatga aactcagcat caaggtgttg ctccagtcgg ctctgagcct gggccgcagc 180  
 ctggatcggg accgatcccc ctgacagcag ttctttgtag tgatggagca ctgctcaca 240  
 catgggctga aagttaagaa gagttttatt ggccaaaata aatcattctt tggctccttg 300  
 gagctggttg agaaactttg tcagaagaca tcagatagat cgactagtgt cagaatctct 360  
 ccagaattaa agacagctgt ggaagagggc cgagcgtggc cactatctgc actcatgcaa 420  
 aagaaactgg cagattatct gaaagtcctt atagacaata aacatctctt aagcgagttc 480  
 tatgagctgg aggtcttaat gatggaggaa gaagggatgg tgattgttgg tctgtggtg 540  
 ggaactcaat ttctcgatgc caatctctgc ttgaaaggag aagacttgga ttctcaggtt 600  
 ggagtaatat attttccctt ctaccttaag gatgtgcagg atcttgatgg tggcaaggag 660  
 catgaagaag ttactgatgt ccttgatcaa aaaaattatg tggaaagact taaccggcac 720  
 ttgagctgca cagttgggga tcttcaaacc aagatagatg gcttggaaaa gactaactca 780  
 aagctccaag aagagctttc agctgcaaca gaccgaattt gctcaactca agaagaacag 840  
 cagcagttaa gagacaaaaa tgaattaatc cgagaagaaa gtgaaaagag tgtagagata 900  
 acaaaacagg ataccaagtg tagctggag acttacaagc aaactcggc aggtctggatg 960  
 gaaatgtaca gtgatgtgtg gaagcagcta aaagaggaga agaaagtcgg gtggaaactg 1020  
 gaaaaagAAC tggagttaca aattggaatg aaaaaccgaaa tggaaatgac aatgaagtta 1080

ctgtgaaaagg acaccccaga gaagcaggac acactagttg cccctccgcc a gc 1132

<210> 257

<211> 519

<212> DNA

<213> Homo sapiens

<400> 257

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tctgtacgtg ggggacctgc accccgacgt gaccgaggcg atgctctacg agaagttcag 120  
cccgccggcg cccatcctct ccatccgggt ctgcaggggac atgatcaccc gccctcctt 180  
gggctacgog tacgtgaact tccagcagcc ggcggacgog gaacgtgctt tggacacccat 240  
gaattttgat gttataaaagg gcaagccagt acgcatcatg tgggtctcagc gtgatccatc 300  
acttcgcaaa agtggagtag gcaacatatt cattaataat ttggacaaat ccatcgacaa 360  
taagcacta tatgatacgt ttctgcgtt tggtaacatc ctttcatgta aggtgggttg 420  
tgatgaaaaa ggctccaagg gctatggatt tgtacacttt gaaacacagc aagcagctga 480  
aagagctatt gaaaaaatga atgggatgct tctaaatga 519

<210> 258

<211> 596

<212> DNA

<213> Homo sapiens

<400> 258

gctttgcaaa agacttagaa gctaagcaga aaatgagctt aacatcctgg tttttggtga 60  
gcagtggagg cactcgccac aggtcgccac gagaatgat tttttgttga agagatgact 120  
gtgagctcat gttgcagtct cgtagtgtgg ataaagcaaca cgtctcctac aactatgatg 180  
cgtctacgga tgagcattta gtgaaggatt tgggcagcct caatgggagc tttgtgaagt 240  
atgtaaggat tccggaaacag acttatatca ccttgaaact tgaagataag ctgagatttg 300  
gatatgatgc aaatcttttc actgtagtac aaggagaaat gaggggtccct gaagaagctc 360  
ttaagcatga gaagtttacc attcagcttc agttgtccca aaaatcttca gaatcagaat 420  
tatccaaatc tgcaagtgcc aaaagcatag attcaaaagt agcagacgct gctactgaag 480  
tgacgacaaa aactactgaa gcaatgaaat ccgaggaaaa agccatggat atttctgcta 540  
tgccccgtgg tactccatta tatgggcagc cgtcatgggt gggggatgat gaggtg 596

<210> 259

<211> 595

<212> DNA

<213> Homo sapiens

<400> 259

gaattcggca ccagagaaaa agcttcaagg tatattgagt cagagtcaag ataaatcaact 60  
tcggagaatt tcagaattaa gagaggagct gcaaatggag cagcaagcaa agaaccatct 120  
tcaggacgag ttgtgatcat gtttggagga gaaagatcag tatatcagtg ttctccagac 180  
tcaggtttct ctctctaaagc agcgattaca gaatggccca atgaatgttg atgctcccaa 240  
accctccct cccggggagc tccaggcaga agtgcacggt gacacggaga agatggaggg 300  
cgtcggggaa ccagtgggag gtgggacttc cgctaaaaac ctggaaaaatg tccagcaaaag 360  
agtgaacagt caggagaatc tgcttcacgag ctgtaaaggag acaattgggt cccacaagga 420  
gcagtcgcga ctgctgctga gtgagaagga ggcactgcag gagcagttgg atgaaaggct 480  
gcaggagctg gaaaagatga aggggatggt aataaccgag acgaagcgcc aaatgcttga 540  
gaccttgaaa ctgaaagaag atgaaattgc tcagcttcgt agtcatatca aacag 595

<210> 260

<211> 994

<212> DNA

<213> Homo sapiens

<400> 260

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gaattcgcca cgaggcgctg cctgcctctt tgctgtctat cagcctttct tgcctcttcc 60
ttttcgctct cctctgttct ccttttctca aacaaacaag acatggcaaa ccgcagtccta 120
accacgcccc ttgaaaattat ccatagtttt acagacagct ccaggccatg agccacaatg 180
tccaaaaatta ttcttgagca ctgatataaa ttacttagac ctctcttgag ggcagaactc 240
agctgttgcct ctcatgtgct gcagtgctgg aaagggttct ggtatgtcct caaaatgagt 300
ccacgagttt actgagtgct tacaggtaaa ggaatgaata taagatgtct ttctgatcag 360
aacaggtgtc cctctcacatg agctttacta gactctggga gggaaaagta gccagtaact 420
tctgaaccat tttttaaatc ttgttttctc atggtgaaat tatagcagtt atcccaaat 480
gttttaatta tcaaaatact gtctttttaa aaaaaaaaaa agtaaacctt tttaaacgat 540
tagatttcaac ttgggtttct tttccaaaaa atgctaggta gacaaggcat tgaatacatg 600
agtttccttt aagaaccatc agaataataa ttaaacatga agaaaaactgc tatatctagt 660
agaataataa tctaaagttt acaactaaaa gtacctcac agaataagca ataccttct 720
gttctggaca tgggttcaaa ttgaatatg gaaataattt ccttggaagt ccctagaggg 780
aggctcaggg aagtatgcat taagaggtaa aggagagaat ggaataaaa gtcaactataa 840
tgcagattta tgccttattt tttagcattt tttaaatgtt ggtgttttca aggtgttttt 900
tgctttttat tagatctata taaataagtt aactagcaat tttagtttgt atttaagcta 960
cacttaatct ttttcttgg tgatatttat ttct 994

```

&lt;210&gt; 261

&lt;211&gt; 594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (538)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 261

```

gaattcgcca ccagtgagga tccagctgaa ccatgccaac cgccaggctg cggaggcaat 60
caggaacctt oggaacacccc agggaatgct gaaggacaca cagctgcacc tggacgatgc 120
tctcagcagc caggacgacc tgaagagca gctggccatg gttgagcgca gagccaacct 180
gatgcaggct gagatcgagg agctcaggcc atccctggaa cagacagaga ggagcaggag 240
agtggccgag caagagctac tggatgccag tgagcgctg cagctctccc acacccgaa 300
caccagctc atcaacacca agaagaagct ggagacagac atttcccaaa tccagggaga 360
gatggaagac atcgtccagg aagcccccaa cgcagaagag aaggccaaga aagccatcac 420
tgatgccccc atgatgcccg aggagctgaa gaaggagcag gacaccagcg cccacctgga 480
gcgatgaag aagaacatgg agcagacctg gaaggacctg cagcaccgtc tggacgancg 540
tgagcagctt ggcgtgaag ggcgggcaag aagcagatcc agaaactgga ggct 594

```

&lt;210&gt; 262

&lt;211&gt; 594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 262

```

gaaaaggagg ctggagccaa aggcatagtc agggtaaatg ctcttttttc tttatcccaa 60
atcagatagt gtttaggctt ttctatcaaa tataaaaacc cagccaggtt catggctcat 120
tcggcagcaa cctgagacg ctttacagct cttagcccta aaaggctcaaa agggcgctct 180
atgctcaata tacattttat tacccaatct gccccggaca ttaataaaaa ctccaaaaat 240
taaatccggc cctcaaaccc cacaacagga cttaattgac ctacaccttca aggtgtagaa 300
taataaaaaa aaaaagttgc aattccttgc ctccgtgtg atcacaaccc cagccacatc 360
tcagcacac aagaacttcc aaacgcttga accacagcag ccaggcgctc ctccagaacc 420
tctctcccca ggaagctgct acatgtgccg gaaatctggc catctgtgag ccataggcca aggaatgcct 480
gcagcccccg attcctccta agcctgttcc catctgtgag ggaccccact gaaaatcgga 540
ctgttcaact cacctggcag ccactctcag agaccctgga actctggccc aagg 594

```

&lt;210&gt; 263



```

<211> 506
<212> DNA
<213> Homo sapiens

<400> 263
gaattcggca cgagcggaaa cttaggggcc acgtgagcca cggccacggc cgcataggca 60
agcacccgaa gcaccccgcc gcccgcggtg atgctgggtg tctgcatcac caccggatca 120
acttcgacaa ataccaccca ggctactttg ggaaagtgtg tatgaagcat taccacttaa 180
agaggaccca gagcttctgc ccaactgtca accttgacaa attgtggact ttgtgcagt 240
aacagacacg ggtgaatgct gctaaaaaca agactggggc tgctccatc attgatgtgg 300
tgcgatcgcc ctactataaa gttctgggaa agggaaagct cccaaagcag cctgtcatcg 360
tgaaggccaa attcttcagc agaagagctg aggagaagat taagagtgtt gggggggcct 420
gtgtcctggt ggcttgaagc cacatggagg gagtttcatt aaatgctaac tactttttaa 480
aaaaaaaaa aaaaaaaaaa ctcgag                                     506

<210> 264
<211> 600
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (32)
<223> n=A,T,C or G

<400> 264
ggctcgtgaa cacacactga cagctatagg gnaggcggcg gcacgcgtcc cgttccct 60
ggcggcgggg gtgtcccgtc gccggccctg aagtaccca taacatgtc ttgtgagagg 120
aaaggcctct cggagctcgc atcggagctc tacttcccca tcgcccggtt cctggaagat 180
ggaccctgtc agcaggcgcc tcagggtgct atccgcgagg tggccgagaa ggagctgctg 240
ccccggcgca ccgactggac cgggaaggag catcccagga octaccagaa tctggtgaag 300
tattacagac acttagcacc tgatcacttg ctgcaaatat gtcatcgact aggcactctt 360
cttgaacaag aaattcctca aagtgttctt ggagtacaaa ctttattagg agctggaaga 420
cagtcctttc tacgcacaaa taaaagctgc aagcatgttg tgtggaagg atctgctctg 480
gtgcgcttgc actgtggaag accacctgag tcaccagtta actatggtag cccaccagc 540
attgcggata ctctgttttc aagggaagct aatgggaaat acagacttga gcgacttgtt 600

<210> 265
<211> 534
<212> DNA
<213> Homo sapiens

<400> 265
gaattcggca cagagtggga gcccatcatg gcgacgcccc ctaagcggcg gccggtggag 60
gccacggggg agaaagtgtc gcgctacgag accttcatca gtgacgtgct gcacggggac 120
ttgcgaaaag tgctggacaa tcgagacaag gtatatgagc agctggccaa atacctcaa 180
ctgagaaatg tcaattgagcg actccaggaa gctaagcact cggagttata tatcgaggtg 240
gatttgggct gtaactctct cgttgacaca gtggtccagc atactcaag catctatgtg 300
gcctgggat atggtttttt cctggagttg acactggcag aagctctcaa gttcattgat 360
cgtaagagct ctctctcac agagctcagc aaagcctca ccaaggactc catgaattac 420
aaagcccata tcacatgttt gctagagggg cttagagaaac tacaaggcct gcgaatttc 480
ccagagaagc ctcacatttg acttcttccc cccatcctca gacattaaag aggc                                     534

<210> 266
<211> 552
<212> DNA
<213> Homo sapiens

```

```

<400> 266
gaattcggca ccagggcacc tccgcctcgc cgcgcctagg tggccgggt cgcggcggt 60
gcgcctagg atgaatatca tggacttcaa cgtgaagaag ctggcgccg acgcaggcac 120
cttcctcagt cgcgcctgtc agttcacaga agaaaagcct ggccaggctg agaagacaga 180
attggatgct cacttagaga acctccttag caaagctgaa tgtaccaaa tatggacaga 240
aaaaataatg aaacaaactg aagtgttatt gcagccaaat ccaaatgccca gcatagaaga 300
atttgtttat gagaaactgg atagaaaagc tccaagtcgt ataaacaacc cagaactttt 360
gggacaatat atgattgatg cagggaactga gtttggccca ggaacagcctt atggtaatgc 420
ccttattaaa tgtggagaaa cccaaaaaag aattggaaac gcagacagag aactgattca 480
aacgtcagcc ttaaattttc ttactccttt aagaaacttt atagaaggag attacaaaa 540
aattgctaaa ga 552

```

```

<210> 267
<211> 551
<212> DNA
<213> Homo sapiens

```

```

<400> 267
gaagcctacc agccagggtgc cggccccccc acccccgcc cagccccctc ctgcagcggt 60
ggaagcggct cggcagatcg agcgtgaggc ccagcagcag cagcacctgt accgggtgaa 120
catcaacaac agcatgcccc caggacgcac gggcatgggg accccgggga gccagatggc 180
cccgtgagc ctgaatgtgc ccgcacccaa ccaggtagc gggcccgctca tgcccagcat 240
gctcccggg cagtggcagc aggcgcccc tccccagcag cagcccatgc caggcttggc 300
caggcctgtg atatccatgc aggcgccagg ggcgtggct gggcccgga tgcccagcgt 360
gcagcaaccc aggagcatct cccccagcgc tctgcaagac ctgctgcgga ccttgaagct 420
gccagctcc ctcagcagc aacagcaggt gctgaacatt ctcaaatcaa acccgagct 480
aatggcagct ttcatcaaac agcgcacagc caagtacgtg gccaatcagc ccggcatgca 540
gccccagcct g 551

```

```

<210> 268
<211> 573
<212> DNA
<213> Homo sapiens

```

```

<400> 268
gaattcggca ccagggttcc ttgtgggcta gaagaatcct gcaaaaatgt ctctctatcc 60
atctctcgaa gacttgaagg tagacaaagt aattcaggct caaactcgtt ttctgcgaaa 120
ccctgccaat ccagcaatatt tgtcagaagc ttctgctcct atccctcacg atggaaatct 180
ctatcccaga ctgtatccag agctctctca atacatgggg ctgagtttaa atgaagaaga 240
aatacgtgta aatttggcgc tggtttctgg tgcaaccact caggggcagt tggtagcaag 300
accttccagt ataaactata ttgtggctcc tgaactggt aatgatgttg gaattcgtag 360
agcagaaatt aagcaaggga ttctgtaagt cattttgtgt aaggatcaag atggaaaaat 420
tggactcagg cttaaatcaa tagataatgg tatatttgtt cagctagtcc agggctaattc 480
tcagcctca ttggttggtc tgagatttgg ggaccaagta cttcagatca atggtgaaa 540
ctgtgcagga ttgagctctg ataaagcgca caa 573

```

```

<210> 269
<211> 500
<212> DNA
<213> Homo sapiens

```

```

<400> 269
gaatcggcac caggaaacct ttattagcag agatagcttg cttggatcag attacgggga 60
atgtggggga gccatgagga aactaactaa aggggagcct ttggggacca gggggagaca 120
agtcactatt ttgagggaga aagctctgga ttgattctga caggacactt gagtgtgaac 180
tgtccaagct aagcctcttg gtgtgtagag agagccctta cagatagata gcacctttg 240
tttcagagtg gaaggactag ccactaagga ccagaccaag atgcatgtag ctgactgaca 300
agcacctgat gaagaggagg ggtctcctcc aagtttgtgt ttggaactcc tctctgtgtc 360

```

```

aatttctctaa aagccataat ccagcaagct gaactcatga gaaggtctgc ttcattgtga 420
gcattggaaga cagaacacag acggaaactg cagtcatggt gtgaagacac cacgcatagg 480
ttaggggcgag ttaggaggaa

```

&lt;210&gt; 270

&lt;211&gt; 224

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 270

```

gaattcggca cgagaagact acaatctcca gggaaacctg gggcgtctcg cgaaacgtc 60
cataactgaa agtagctaa gacccaccgc cggagggaagt gagctctctc gggcgtgggt 120
tgttcgtgat ccttgcatct gttacttagg gtcaaggctt gggctcttgc ccgcagacc 180
ttgggacgac ccggcccccag cgcagctatg aacctggagc gagt

```

&lt;210&gt; 271

&lt;211&gt; 447

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 271

```

gaattcggca cgaggctggg ccgggcccga gcgcatcgcg ggctcgggct ggggggctcc 60
ggctcgggct gctgggcccgc gaggcgccga gcttgggagc ggagcccagg ccgtgccgcg 120
cgcgcccatg aaggcgcaagg aggagaagga gggcgggcga cggtcgggct ctggcgccgcg 180
aagccccgag aagagcccga gcgcgcagga gctcaaggag cagggcaatc gctcttctgt 240
ggggccgaaa tactccggag cgcgccgctg ctacggccgc gcgatcacc ggaaaccgct 300
ggtgcccgctg tattcaccca accgggcctt gtgtaacctg aagatgcagc agcacagaga 360
ggccctggcc gactgcggcg gcgcctcgga gctggacggg cagtctgtga aggcgcactt 420
cttcctgggg cagtgcagc ttgagat

```

&lt;210&gt; 272

&lt;211&gt; 606

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 272

```

gcaactactt atattccttt gatggataat gctgactcaa gtccgtgtgt agataagaga 60
gaggttattg atttgcttaa acctgaccaa gtagaaggga tccagaaatc tgggactaaa 120
aaactgaaga ccgaaactgt caaagaaat gctgaagtga agtttaaaga tttcttctgt 180
tccttgaaga ctatgatgtt ttctgaagat gaggtctctt gtgtgtgtaga cttgtcaaa 240
gagaagtctg gtgtataaca agatgcttta aagaagtcaa gtaagggaga attgactacg 300
ctatacatc agcttcaaga aaaggacaag ttactcgtcg ctgtgaagga agatgctgct 360
gctacaaaag atcggtgtaa gcagtttaacc caggaatga tgacagagaa agaaagaagc 420
aatgtggtta taacaaggat gaaagatcga attggaacat tagaaaaaga acataatgta 480
tttcaaaaca aaatacatgt cagtatatca gagactcaac agatgcagat gaagtctcag 540
caagttcgtg agcagatgga ggcagagata gtcacttga agcaggaaaa tgggtatact 600
ggagaa

```

&lt;210&gt; 273

&lt;211&gt; 598

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 273

```

gaattcggca ccaggcccgg tcccgcggtc gcagctccag ccgctctctc cgcgcagccg 60
ccgcctcagc tgcctcgtct gtgggtcggt cctctccggc acttgggctc cagtcgcgcg 120
ctccaaagccc ttcaggccgc ccagtgctc tcctctctc ccggccagac ccagcccgcg 180
gaagatgggt gaccgcgagc aactggtgca gaaagcccgc ctggccgagc aggcggagcg 240

```

```

ctacgacgac atggcgccg ccatgaagaa cgtgacagag ctgaatgagc cactgtcgaa 300
tgaggaaaca aaacctctgt ctgtggccta caagaacgtt gtggggggcac gccgtcttct 360
ctggagggtc atcagtagca ttgagcagaa gacatctgca gacggcaatg agaagaagat 420
tgagatgttc cgtgcgtacc gggagaagat agagaaggag ttggaggctg tgtgccagga 480
tgtgtgagc ctgctgagata actacctgat caagaattgc agcgagaccc agtacgagag 540
caaagtgttc tacctgaaga tgaaaggga ctactaccgc tacctggctg aagtggcc 598

```

&lt;210&gt; 274

&lt;211&gt; 536

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 274

```

gcaccaagag actaaacaag aaagtggatc agggaagaag aaagcttcat caaagaaaca 60
aaagacagaa aatgtcttcg tagatgaacc ccttattcat gcaactactt atattccttt 120
gatggataat gctgactcaa gtctgtggtt agataagaga gaggttattg atttgcctta 180
acctgaccaaa gtagaaggga tccagaaatc tgggactaaa aaactgaaga ccgaaactga 240
caaagaaaaa gctgaagtga agtttaaaga ttttcttctg tctctgaaga ctatgatgtt 300
ttctgaagat gaggctcttt gtgttgtaga ctgtctaagg gagaagtcct gtgtaataca 360
agatgcttta aagaagtcaa gtaagggaga attgactacg cttatacatc agcttcaaga 420
aaaggacaag ttactcgctg ctgtgaagga agatgctgct gctacaaagg atcgggtgaa 480
gcagtttaacc caggaaatga tgacagagaa agaagaagc aatgtggtta taacaa 536

```

&lt;210&gt; 275

&lt;211&gt; 494

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (379)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 275

```

gaattcggca ccagggtcgc ggttcttgtt tgtggatcgc tgtgatcgct acctgacaat 60
gcagatcttc gtgaagactc tgactggtaa gaccatcacc ctcgagggtt agcccaagtga 120
caccatcgag aatgtcaagg caaagatcca agataaggaa ggcacccctc ctgaccaagca 180
gaggctgctc ttgtctgtaa aacagctgga agatggcgcc accctgtctg atacacaact 240
ccagaaagag tccacctcgc acctggtgct ccgtctcaga ggtgggatgc aaactcttgt 300
gaagacactc actggcaaga ccatcacctc tgaggtggag cccagtgaca catcgagaa 360
cgtcaaaaga aagatccang acaaggaagg cattctcctc gaccagcaga ggttgatctt 420
tgccggaagc agctgggaag atgggcgcac cctgtctgac tacaacatcg agaaagagtc 480
tacctcgac cttg 494

```

&lt;210&gt; 276

&lt;211&gt; 484

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 276

```

ggcttttaac cagaagtcaa acctgttcag acagaaggca gtcacagcag aaaaatcttc 60
agacaaaaag cagtacacag ttgtcaggga gtgtgggcga ggccttagca ggaagtcaca 120
gtcctatcata caccagagga cacacacagg agaaaagcct tatgtctgag gagagtgtgg 180
gcgaggcttt atagttgagt cagtctctcg caaccacctg agtacacact ccggggagaa 240
accttatgtg tcagccattc gtggcgaggc ctttagctgc aagccatacc tcactcagaa 300
tcagaggagca cacacagagg agaatacggt tatgtgcaca ggtgtgtggc gaggtctttc 360
tgaaaagtca gagctcatta agcaccagag aattcacacg ggggataagc cttatgtgtg 420
cagagattga ggccgaggct ttgtaaggga gatcatgtct caacacacac cagaggatta 480

```

catt

484

<210> 277  
 <211> 513  
 <212> DNA  
 <213> Homo sapiens

<400> 277  
 gcttgagcct gccaatcaga gcttggcaga gctgagagat cagcggcagg gggagcgcct 60  
 ggaacatgca goagctttgc gggccctaca agatcaggta tccatccaga gtgcagatgc 120  
 acaggaacaa gtggaaggcc ttttggctga gaacaatgcc ttgaggacta gcctggctgc 180  
 cctggaggcag atccaaacag caaagaccga agaactgaat atgctccggg aacagaccac 240  
 tgggctggca gctgagttgc agcagcagca ggctgagtag gaggacctta tgggacagaa 300  
 agatgacctc aactcccagc tccaggagtc attacgggcc aatagctcac tgctggaaac 360  
 acttcaagaa ataggcgagg agaaggagca gttgacccag gaattacagg aggcctcgaa 420  
 gagtgcggag aagcgggaagg ccatgcttgg atgagctagc aatggaaaac ctgcaagaga 480  
 agtcccacac aaggaagagc ttgggagcag ttc 513

<210> 278  
 <211> 471  
 <212> DNA  
 <213> Homo sapiens

<400> 278  
 gaattcggca ccagccaagg ccctgtccct ggctcgggcc cttgaagagg ccttggaaac 60  
 caaagaggaa ctgagcgagg caacacaaat gctcaaaagg gaaatggaag acctgggtcag 120  
 ctccaaggat gacgtgggca agaactgcca tgagctggag aagtcacaag gggccctgga 180  
 gacccagatg gaggagatga agacgcagct ggaagagctg gaggacgagc tgcaagccac 240  
 ggaggagccc aaactgcgcc tggaaagtcaa catgcaggcg ctcaaggggcc agttcgaaag 300  
 ggatctccaa gcccgggagc agcagaatga ggagaagagg aggcacactgc agagacagct 360  
 tcacgagtat gagacggaac tggaaagcga gcgaaagcaa cgtgccctg cagctgcagc 420  
 aaagaagaag ctggaagggg acctgaaaga cctggagcct caggccgact t 471

<210> 279  
 <211> 497  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (457)  
 <223> n=A,T,C or G  
 <221> misc\_feature  
 <222> (471)  
 <223> n=A,T,C or G

<400> 279  
 gaattcggca cgaggccaca gaggcggcgg agagatggcc ttcagcgggt cccaggctcc 60  
 ctacctgagt ccagctgtcc ccttttctgg gactattcaa ggaggtctcc aggcaggact 120  
 tcagatcact gtcaatggga ccgttctcag ctccagtgga accaggtttg ctgtgaactt 180  
 tcagactggc ttcagtggaa atgacattgc cttccacttc aacctcgggt ttgaagatgg 240  
 agggtagctg gtgtgcaaca cgaggcagaa cgaaagctgg gggcccgagg agaggaagac 300  
 acacatgcct ttccagaagg ggaatgccct tgacctctgc ttctctgtgc agagctcaga 360  
 ttcaaggtg atggtgaacg ggaatcctct cgtgcagtag ttccaccggc tgcccttcca 420  
 ccgtgtggac accatctcgg tcaatggctc tgtgcantct tctacatca ncttcagac 480  
 ccagacagtc atccaca 497

<210> 280

<211> 544  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (451)  
 <223> n=A,T,C or G

<400> 280  
 gaattcggca ccagaatagg aacagctcgg gtctacagct cccagcgtga gcgacgcaga 60  
 agacgggtga ttctctgatt tccatctgag gtacccgggt catctcacta gggagtgcca 120  
 gacagtgggc gcagggccagt gtgtgtgctg accgtgcgag agccgaagca gggcgaggca 180  
 ttgcctcacc tgggaagcac aagggggtcag ggagttccct ttccagagta aagaaagggg 240  
 tgacggagcg acctggaaaa tcgggtcact cccaccgaa tattgtgctt ttcagaccgg 300  
 cttaaagaaac ggccgaccac gagactatat cccacacctg gctcagaggg tctacgccc 360  
 acggaatctc gctgattgct agcacagcag tcttagatca aactgcaagg ggggcaacga 420  
 ggctggggga gggcgcccg ccattgccca ngcttgctta ggtaaacaaa gcagccggga 480  
 agcttgaact ggggtggagcc caccacagct caaggaggcc tgcctgcctc tgtagctcca 540  
 cctc 544

<210> 281  
 <211> 527  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (456)  
 <223> n=A,T,C or G

<400> 281  
 gaattcggca cgaggcctcg ctacagctcca acatggcaaa aatctccagc cctacagaga 60  
 ctgagcgggt catcgagctc ctgattgctg tcttccagaa gtatgtgtga aaggatgggt 120  
 ataactacac tctctccaag acagagttcc taagcttcat gaatacagaa ctagctgcct 180  
 tcacaaagaa ccagaaggac cctggtgtcc ttgaccgcat gatgaagaaa ctggacacca 240  
 acagtgatgg tcagctagat ttctcagaat ttcttaatct gattggtggc ctgactatgg 300  
 cttgccatga ctctctctc aaggctgtcc cttcccagaa gcggacctga ggaccctctg 360  
 gcctggcct tcacaaaccac cccctttcct tccagccttt ctgtcatcat ctccacagcc 420  
 caccatcccc ctgagcacac taaccacctc atgcanggcc cccctgccaa tagtaataaa 480  
 gcaatgtcct tttttaaaaa atgaaaaaaa aaaaaaaaaa actcgag 527

<210> 282  
 <211> 514  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (494)  
 <223> n=A,T,C or G

<400> 282  
 ggaagactgg agccttttgc gcggcgctgc cctccctcgt gtccccgcga gctcggaggg 60  
 cccgctcgtg gctgcggggg ccccgaggag ttgaaaaacta agcatgggga agagctgcaa 120  
 ggtggtcgtg tgtggccagc cgtctgtggg caaaacttca atctcggagc agcttctgta 180  
 tgggaacctt gtagtggttt cggagatgat cgagacgcag gaggacatct acgtgggctc 240  
 cattagagca gaccgggggg tgcgagagca ggtgcgtttc tatgacaccg gggggctccg 300

```

agatggggcc gaactgcccc gacactgctt ctcttgcact gatggctacg tctgtgtcta 360
tagcacagat agcagagagt cttttcagcg tgtggagctg ctcaagaagg agattgacaa 420
atccaaggac aagaaggagg tcaccatcgt ggtccttggc aacaagtgtg acttacagga 480
gcagcgcgct gtanacccaa atgtggctca acac 514

```

```

<210> 283
<211> 484
<212> DNA
<213> Homo sapiens

```

```

<400> 283
ggcgggggcg tggacagtca tggcgggccg gcgcggggct ctcatagtgc tggagggcgt 60
ggaccgcgcc ggggaagagca cgcagagccg caagctgggt gaagcgctgt gcgcgcggg 120
ccaccgcgcc gaactgctcc ggttcccgga aagatcaact gaaatcgga aacttctgag 180
ttcctacttg caaaagaaaa gtgacgtgga ggatcaactg gtgcacctgc ttttttctgc 240
aaatcgctgg gaacaagtgc cgttaattaa ggaagaattg agccaggcgc tgacctctgt 300
cgtggacaga tacgcathtt ctggtgtggc cttaccgggt gccaaaggaga atttttccct 360
agactggtgt aaacagccag acgtgggcct tcccaaaccc gacctggctc gtttccctca 420
gttacagctg gcggtatgct ccaagcgggg agcgttttggc catgagcgct atgagaacgg 484
ggct

```

```

<210> 284
<211> 514
<212> DNA
<213> Homo sapiens

```

```

<400> 284
gaattcgcca cgagcgcgag gccgcggagg ctctcggtc cttcagcacc cctcggcccg 60
acgcaccacc gccctcacc ccccgagagc cgaagaatgga cccaagtggg gtcaaaagtgc 120
tggaaacagc agaggacatc caggagaggg gccagcaggt cctagaccga taccaccgct 180
tcagggaact ctcaaccctt agcgctcaga agctggaaga ttccatcaga ttccagttct 240
ttcaaaagga tgctgaagag ctggagaaat ggatacagga aaaacttcag attgcattcg 300
atgagaatta taagaccaca accaacttgc agggaaagct tcagaagcat caagcatttg 360
aagctgaagt gcaggccaac tcaggagcca ttgttaagct ggatgaaact ggaaacctga 420
tgatctcaga agggcatttt gcatctgaaa ccatacggac ccgtttgatg gagctgcacc 480
gcagtgggga attacttttg gagaagatgc gaga 514

```

```

<210> 285
<211> 383
<212> DNA
<213> Homo sapiens

```

```

<400> 285
gaattcgcca cgagcgcgag gccgcggagg ctctcggtc cactctggcg accgcccccg 60
gggccccccg cgcggcgccg gcgcccgcga tggcgaggga ggactactat ctggagctgt 120
gcgagcgccc ggtgcagttc gagaaggcga accctgtcaa ctgcgtctct ttogatgag 180
ccacaagaga ggtttttgct gttcgtatct gtggagctac tggcggtgga gttaaaggcc 240
cagatgatag gaatcccatc tcatttagaa tggatgacaa agggagaagt aagtgcatta 300
agttttcctt agaaaataag atattggctg ttcagaggac ctcaaaagact gtggattttt 360
gtaattttat ccctgataat tcc 383

```

```

<210> 286
<211> 943
<212> DNA
<213> Homo sapiens

```

```

<400> 286
gaattcgcca ccagggccgt ggcgggaggg gagcgctgca cggtggagcg tggggccgac 60

```

```

ctcacctacg cggagttcgt gcagcagtac gtgcgcccc gatcgcgagg gtgcgctcct 120
gttcaccggc cegtctgccc gcagccgccca aggcgcgcct cccctgacct cgcgcgcacg 180
cgtggggctg gggcgcgag gctggcggtc cggcctggcc gcgactctgc cctctcttcc 240
agaggtctcg gggcctgtgc tcccgcgaca ggttgctggc ttgctttggg gacagagtgg 300
tcgggtcgtg caccgccaac acctactcct accacaaagt ggacttgccc ttccaggagt 360
atgtggagca gctgctgcac cccaggacc ccacctccct gggcaatggt gaggcagccc 420
taggcggcgg taggggggtg ggaagcttgg agtctccagg tgccaggatc cctgtccccg 480
cogtctctgt tggcagacac cctgtacttc ttccggggaca acaacttcac cgagtggggc 540
tctctcttct ggcaactact cccaccccca ttggcctgc tgggaaacgc tccagcttac 600
agctttggaa tcgcagagac tggctcgggg gtgccttccc actggcatgg acccggttac 660
tcagaagtga tctacggtcg taagcgctgg ttccctttacc cactcgagaa gacgcagag 720
ttccaccoca acaagaccac actggcctgg ctccgggaca cataccagc cctgccacgc 780
tctgcacggc ccctggagtg taacctccgg gctgggtgag tgcgtgactt ccccgaccgc 840
tggtggcatg ctacgctcaa ccttgacacc agcgtcttca tctccacctt cctcggttag 900
ccaaaacacg tggcaggact gccggtcaca caccagcacg tcc 943

```

&lt;210&gt; 287

&lt;211&gt; 1143

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 287

```

gaattcgcca cgaggggaaga acagctgttg gaacaacaag aatatttaga aaaagaaatg 60
gaggaagcaa agaaaatgat atcaggacta caggccttac tgcctcaatg atccttacct 120
gaagatgaac aggaagagcc cttggccctc tgtgaacagg gtgtcaatcc cgaggaacaa 180
ctgattataa tccaaagtcg tctggatcag agtatggagg agaatacagg cttaagaaga 240
gaactcgtga aatgtaaaaca agaagccaga aacttacagg ggataaagg tgccttgcag 300
cagagattga ctacgacgga cacatctgtt cttcagctca aacaagagct actgagggca 360
aatattgcca aagatgagct gcaacaaccg aatgtggatc tgacagggaa gctagtgag 420
aggaacccgc tcttgggaga atataaaaa gagctggggc agaaggatcg cctctctcag 480
cagcaccagg ccaagttaga agaagcactc cggaaactct ctgagtgcag ttaccaccag 540
gtggatctag agcgagagct agaacacaaa gatgtcctct tggctcactg tatgaaaga 600
gaggcagatg aggcgaccaa ctacaacagt cacaactctc aaagcaatgg tttctcctt 660
ccaaacggcag gaaaaggagc tacttcagtc agcaacagag ggaccagcga cctgcagctt 720
gttcgagatg ctctccgcag cctgcgcaac agcttcagtg gccacgatcc tcagcaccac 780
actattgaca gcttggagca gggcatttct agcctcatgg agcgcccgca tgttatggag 840
acgcgaagaa aacaagaaag aaaggttcgg gtcaagtccac ccagaaactca agtaggtagt 900
gaataccggg agtccgtggc ccttaactca aagttgctc actcaacag ctctccaact 960
gtcagcagcta cctgtactaa agtgccttat ttcaactgac ggtcaactac gcccttcagt 1020
gtcaatatac caaagaggtt ggaggagggt acgttaaaag attttaaaag agctattgat 1080
cgggaaggaa atcaccggtg tcacttcaaa gcactggatc ctgagtttgg cactgtcaaa 1140
gag 1143

```

&lt;210&gt; 288

&lt;211&gt; 881

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 288

```

gtgagagcgg gccgaggaga ttggcgacgg tgcgccccgt gtttctgttg gcgggtgcct 60
gggctggttg gaacagcgcg ccgaaggaa gaccatgatt tgcgccccgc agttgttggg 120
tgagttaatg ggccgggacc gaaacctagc cccggacgag aagcgacga acgtgcgggtg 180
ggaccacgag agcgttttga aatattatct ctgtggtttt tgcctcgccg aattgttacc 240
aaatacacgt tcatgacttg gtcctgttga aaaaattcat aaaaattcat tgcagaaaaa 300
gtatgagaag agctctcgtt tcatgaaagt ttgctatgag agagattttt tgcgataact 360
acagagctta cttgcagaag tagaacgtag gatcagacga ggccatgctc gtttggcatt 420
atctcaaaac cagcagctct ctggggcgcg tggcccaaca ggcaaaaatg aagaaaaaat 480
tcaggttcta acagacaaaa ttgatgtact tctgcaacag attgaagaat tagggtctga 540

```



```

aggaaaagta gaagaagccc aggggatgat gaaattagtt gagcaattaa aagaagagag 600
agaactgcta aggtccacaa cgtcgacaat tgaaagcttt gctgcacaag aaaaacaaat 660
ggaagtttgt gaagtatgtg gagccttttt aatagtagga gatgccagat cccgggtaga 720
tgaccatttg atgggaaaac aacacatggg ctatgccaaa attaaagcta ctgtagaaga 780
attaaaaaaa aagttaagga aaagaaccga agaactgtat cgtgatgagc gtctaaaaaa 840
ggagaagcaa gaaagagaaa aaaaaaaaaa aaaaactcga g 881

```

&lt;210&gt; 289

&lt;211&gt; 987

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 289

```

gaattcggca cgagggactg tggtttcag gaatggtggc gtctcacgct tcttgtgctt 60
tttcttttg ggctccgag cggctggggt tgggggactg ggcaggaggc tccctgtaaa 120
catttggaat tgggtgggg caggggctgg tgttgggcaa agctgggggt ccaggctgga 180
gaagcagggg cccctccaga cgcagccttg ggagactcag catgtgcccc cctccctca 240
tcacagaaca agacaatggt taaaaaccag aacagatgcc cagaaggggg taccatggcc 300
attaccagca tctcagacaa gggcaggctt caaacaggga ggcctgtggc aaccctctcc 360
ctacgtctgg agctgagggg acagggggag ctgagaacaa agagaggaaa gaggagaaaa 420
gcggcggggg aacaggcggg gagcgtgatc ttcttgcctc catcttctc aggggttggg 480
gggtacaaag tcggcggtgg cccatccgcg caggcccgcg tgccctcag aagaggcccg 540
agtctctcag gttgttcttg atgatgacat cggtgacggc gtcaaacacg aactgcacgt 600
tcttggtgtc ggtggcgcac gtgaagtgcg ttagatctc cttggtgtct ttgogcttat 660
tcaggctctc aaacttactc tggatgtagc tggctgcctc atcatatttt ttggccctg 720
tatactcagg gaagcagatg gtcaggggac tgtgtgtgat ctctctctca aacaggctct 780
tcttgttagg gaagagatg atggacgtgt ctgtgaacca cttgttgttg cagatgctat 840
cgaatagctt catgtctctc tgcattcggt tcatctctc gtctcagct agcaccagt 900
cataggcgct caaggctacg cagaagatga tggctgtgac gccctcaaa cagtggatcc 960
actctctccg ctacagccgc tgaccac 987

```

&lt;210&gt; 290

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(300)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 290

```

gattcaagat gtaccceatt gactttgaga aggatgatga cagcaacttt catatggatt 60
tcatgtggc tgcattcaac ctccgggcag aaaactatga cattccttct gcagaccggc 120
acaagagcaa gctgattgca gggaagatca tccagccat tgccaagacc acagcagccg 180
tggttggcct tgtgtgtctg gagctgtaca aggttgtgca ggggcacgca cancttgact 240
ctacangaa tgggtgctct aacttgagcc ctgcctttct ttggtttctc tgaacccctt 300

```

&lt;210&gt; 291

&lt;211&gt; 352

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(352)

&lt;223&gt; n = A,T,C or G

```

<400> 291
aaccaagctg ccaaccggggg tggatcggat cgcgcttgag aggcattctgt ctgccgagga      60
cttctcaagg gtattttgcca tgtccctga agagtttggc aagctggctc tgtggaagcg      120
gaatgagctc aagaagaagg cctctctctt ctgatggccc ccacctgtcc cgggacggcc      180
cccttaccce tgctgtctca gggtttttcc ccggcggggt gggaggggga ggaagtgggg      240
tggaaatnng gtgggcnctt ttcctcagtg agagnggggg gccaaaacct ctgcngtccc      300
cggagnagac tatggacttt ctccccctc acaagntgag gggcctcctg ct      352

```

```

<210> 292
<211> 511
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

```

```

<400> 292
cgcggtggct gcgcactcng cctgagaaac tcggcaagcg cgcagtgtcg actccccggt      60
ctatgcacgg cgcattctcag ctaatccaaa agtaaagtga aaagtattgcc      120
aattccaaat caacatatatt agagaaaaatt ggaaaaaggag aagcttacta cagctttatt      180
tgaggacttt ttaaagaacg ctgggttcta tctgtgagct gcaaatcttg gagcaaaaac      240
cagagacatt gccagagcaa acaagaacag aaatacaaat ggagaactgg tcaaaagaca      300
taaccacacg ttatcttgaa caagaaacta cgggggataaa taaagtagcg canccagatg      360
agcaactgac tatgaattct gagaaaagta tgcattcgaa atccactgaa ttagntaatg      420
aaataacatg ngagaacaca gaattggccag gggcagagat caacgaattt tcanatcatc      480
agttcttatc cagatgatga gtctgtttac t      511

```

```

<210> 293
<211> 526
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(526)
<223> n = A,T,C or G

```

```

<400> 293
gataaaaaga actttaatag aaggcactgt tgtccaaaa cacaataagg gtaagagccc      60
acacggtacc accctgctct cctacttctc aaaccacat ccaccaccca gacaggaggg      120
tgcanacccc acaggaaatt acctcccgga gcactgactg atatttttcc ttaaaacaaa      180
aaaatggctg tctcagacta ataacagaac atcttaagag ctataccagc tattacagcc      240
tggttaatana agcagctttc taanaattcc caagtttata anaggcccaa naaatgcatt      300
tattctgttg tctattaaag ctcctatgaca aggagaaagt tatgagtaaa tccctgggttc      360
atcaggaggt aagagctgtg ngcctcatga ggagttaana gctgtgtgca taagcaggtt      420
caagaaacaa actcctgttt gtttgcctct ttgatgggtc aaaaacatca agctgctttc      480
acctctanga caaaatgctt aaagaattta ctctcatcac cttggg      526

```

```

<210> 294
<211> 601
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

&lt;222&gt; (1)...(601)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 294

acttttaaaag	ccaaatatat	tttttaaaaga	tcatgtcttat	aataagtaaa	ttacncatta	60
aggaacatc	aaaaataagt	agatgaataa	aaagggcacac	tcgaaaaatt	tgagcgcaga	120
aaggacagtt	ctttttgttt	tgtttctaata	gtcgggaagaa	aaagaaagag	atatatttaa	180
atcattgttt	tcaagtgaag	gtttctgtca	gttgaagtag	ttagcaatgg	cttctttttc	240
cccggtgcc	aagcaggtc	ttctctgcgt	gactctctgag	gaggngttca	gtcctctgcc	300
atgtataggc	gatacatcaa	ggcgacggcc	actgcagaga	tgccagggat	caccaggttg	360
gtccaccaac	tggaactaga	atcaatagta	gtgataagag	tttccggagg	cttgtttaac	420
tttggtctgt	catctggatg	gagctcccca	atgatgaatg	ttttggacat	ttccctggca	480
tctgtagant	gcccgcacatc	ctcaaaagttc	tcagtagcng	tcacctccac	ttgttccott	540
aaaacttctt	ccccaccagg	atgctcttcc	agaaaattgg	gncaaatcgn	acacctgtgt	600

g

601

&lt;210&gt; 295

&lt;211&gt; 262

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 295

cccttagccc	caaggccct	gggggcagcc	accctcccgc	ctgtcggccc	gtagatttat	60
caagggtgtt	atggggccag	ctttgggggg	ccagtcccga	tgcaacttga	gggggtgttg	120
agaggggact	ccccactcgc	cacttaactc	aacggctctc	ggggccctggg	gctgttttta	180
ccatgtttgt	ttttgaagct	caggtgtctc	acgtctgggc	tgaccaggcc	gaagagagaa	240
attaagatt	tgaggttttt	cc				262

&lt;210&gt; 296

&lt;211&gt; 598

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(598)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 296

gttagaacia	ctcagcaaaa	taaaattcct	gtttattgtt	ggacaacatt	gtttcacaca	60
tacatcaaac	agggcaaaaa	aaataaacag	caacttcata	gacaaaaaag	gaaaaaaaaa	120
gaaacctttt	atctttggcg	tttttaacca	tctcatacaa	accaactact	tatagtacag	180
ctaagtacat	acacaaaaaa	gttactggaa	tgctcggaa	aagattgttt	ttctgtgtgc	240
atttttgctt	tttttacaag	gntttttttc	tcctttgaga	ttataatgaa	catggncaca	300
ccacaagtaa	agtcagaagt	aggacagana	acgctccgaa	ggctggtttg	gtcatccgan	360
atcattaaaa	atggctgacc	ctaacaatat	gtacaaaaat	ataaaatgta	aataaaaaat	420
acaaacaaat	ttccttttta	aagtaacttt	aagaaaaaaa	gcaggggcctt	ggaagttttg	480
gttctttttt	cctccctctg	tgcaaatctt	catggtttgg	gttgggttgn	gganancocg	540
tgtcatctgc	gggtggcact	gccccgngg	gcgggcgggc	ctctctctcg	aangngac	598

&lt;210&gt; 297

&lt;211&gt; 509

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 297

agaacacagg	tgctgtgaaa	actaccccta	aaagccaaaa	tgggaaagga	aaagactcat	60
atcaacattg	tcgtcattgg	acacgtagat	tcgggcaagt	ccaccactac	tgccatctgt	120

atctataaat	gcggtggcat	cgacaaaaga	accattgaaa	aatttgagaa	ggagggtgct	180
gagatgggaa	agggctcctt	caagtatgcc	tgggtcttgg	ataaactgaa	agctgagcgt	240
gaacgtggta	tcaccattga	tatctccttg	tggaaatttg	agaccagcaa	gtactatgtg	300
actatcattg	atgccccagg	acacagagac	tttatcaaaa	acatgattac	agggacatct	360
caggctgact	gtgctgtcct	gattgttgct	gctggtgttg	gtgaatttga	agctggtatc	420
tccaagaatg	ggcaggagcc	gagagcatgc	ccttctggct	tacacactgg	gtgtgaaaca	480
actaattgtc	ggtgttaaca	aaatggatt				509

<210> 298  
 <211> 267  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(267)  
 <223> n = A,T,C or G

<400> 298						
gggacggggg	aaaggagagc	cttcttctc	ttgctgtctc	tctcggtccc	gagatcagcg	60
gcggcggtga	ccgcgagtgg	gtcggcaccg	tctccggctc	cgggngcnaa	caatgctgac	120
tgatagcgga	ggcgngggca	cctccttnna	ggaggacactg	gactctgtgg	ctccgcgact	180
cggcccaagct	ggggcctcgg	agccgcctcc	gcggggaggg	gtcgggtctgg	ggatccnca	240
cgnaggcctn	tttggggagg	gcggggc				267

<210> 299  
 <211> 121  
 <212> DNA  
 <213> Homo sapien

<400> 299						
ggcaccgagg	ccctcggagc	tctgtttccag	atcgaggtaa	gagggacttt	cttaaaaggcc	60
tagtctatgg	gatggggcgg	cggagggaat	tttttgagaa	ataaaatgaa	gctgcagtgt	120
a						121

<210> 300  
 <211> 533  
 <212> DNA  
 <213> Homo sapien

<400> 300						
aaggtgcaca	gtatttgatg	caggctgctg	gtcttggtcg	tatgaagcca	aacacacttg	60
tccttggatt	taagaaagat	tggttgcaag	cagatatgag	ggatgtggat	atgtatatata	120
acttatttca	tgatgctttt	gacatacaat	atggagtagt	ggttatttcg	ctaaaagaag	180
gtctggatat	atctcatott	caaggacaag	aagaattatt	gtcatcacia	gagaaatctc	240
ctggcaccac	ggatgtggta	gtaagtgtgg	aataatagtaa	aaagtccgat	ttagataactt	300
ccaaaccaact	cagtgaaaaa	ccaattacac	acaaagttaga	ggaagaggat	ggcaagactg	360
caactcaacc	actgttgaaa	aaagaatcca	aaggccctat	tgtgccttta	aatgtagctg	420
accaaaagct	tcttgaagct	agtacacagt	ttcagaaaaa	acaaggaaag	aatactattg	480
atgtctggtg	gctttttgat	gatggagggt	tgaccttatt	gataccttac	ctt	533

<210> 301  
 <211> 560  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature

&lt;222&gt; (1)...(560)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 301

ataaatgac	cottttattg	taagtaatgc	gcaacactgg	cctggctttg	cactgcaagc	60
cctcgggtcaa	gatatagatca	aataactatg	gctgcaggtt	ccacagttcc	acaataacca	120
tggctgcagc	atccacaatt	cagacacaga	catagagctg	gggtgggtgg	aaggggcagg	180
aggggtggcag	agtgcggact	gtccccagcc	ctggcctctc	catgcanagt	tggcccaggc	240
agacacacccc	catggaatga	tgagaaagtg	acggcacggc	cccttccccac	agcaagcctg	300
gggctgcgcag	gaactgccct	tcanaaacctt	tgggcccagg	tcnccctgaa	nccccacaac	360
tttttatctg	gaataagtat	taaaaaacaa	taaattaagc	aaacaacntg	gncttgaag	420
gatgttgacc	nacatggctc	acagtttttg	gcncaaaaaa	ataagggtcg	gtttgctttt	480
tttggaaggc	agggtttgtg	gnttggcttt	caaatnattt	tcaaacccatt	ccccagggag	540
gganaacccc	cgggggggaa					560

&lt;210&gt; 302

&lt;211&gt; 599

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(599)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 302

gcacaaagtac	aaattttattg	gtctggaagt	aaatacaaat	atctcattaa	naaaactctc	60
tggaaagact	tgtgcacaat	agtttcccat	ccgtactcag	cctctcttgc	ccgatcccc	120
gacttttcta	ctcaaaggcca	gggaaggcct	ccaaggngat	gggcggcagg	taacgagtca	180
ttgcctctca	cgccacactg	aaggctggac	tacttctccc	tcaccaactg	ggggtccan	240
aaatcctcgg	gtccccagng	ctgacttaca	atattcaatt	cactctgacc	aaacttccta	300
tganaaaaac	cacgngagc	caaaatgaaa	agtacaaggc	agtagtacag	gaacctggca	360
gcgcactcgg	ccgcccanaa	acgtcagtg	ngctgcccc	ttcgcgaaag	ggtagggag	420
caggaaaaga	ggaagcagga	gagggaaagga	aagtcccatg	gaatatgtat	tccanaatcc	480
ttacattttc	tcagccaccg	ctccccagct	gagttccac	ccccaccccg	acaagaagca	540
aagagtctctg	aggatccaag	aacgtgaccg	ggtcanacan	gttcagctac	tgagttcac	599

&lt;210&gt; 303

&lt;211&gt; 591

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 303

cggagttgta	acgctccact	gactgataga	gcgaccggcc	gaccatggcg	cccggagtg	60
cccgcgggcc	gacgcogtac	tggagggttc	gcctcgggtg	cgccgcgctg	ctcctgctgc	120
tcatcccggt	ggcgcgcg	caggagcctc	ccggagctgc	ttgtttctcag	aacacaaaac	180
aaacctglga	agagtgcctg	aagaacgtct	cctgtcttgc	gtgcaacact	aacaaggctt	240
gtctggacta	ccaggttaca	agcgtcttgc	caccgcttc	cctttgttaa	ttgagctctg	300
cacgtcgggg	agtttgttgc	gtgaactttg	agggcgtgat	catcacactg	tcggtagtgc	360
ggggaaacct	ctcctctggc	attgccatct	gctgctgctg	ctgctcgagg	aggaagagga	420
gcggaaagcc	ggacagaggt	gagggagaag	ccatgcgtga	gcgggagag	agcgagatgc	480
ggcaggagga	acggagagca	gagatgaaga	caagacatga	tgaatcaga	aaaaaatatg	540
gcctgtttaa	agaagaaaac	ccgtatgcta	gatttgaaaa	caactaaagc	g	591

&lt;210&gt; 304

&lt;211&gt; 441

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(441)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 304

gctggacgga	gacctgctgg	aggaggagga	gctggaggaa	gcagaggagg	aggaccgggc	60
gtcgctcgtg	ctgctgtcgc	cgcccgcggc	caccgcctct	cagaccagc	agatcccagg	120
cgggtccctg	gggtctgtgc	tgctgccagc	cgccagggtc	gatgcccggg	aggcggcggc	180
ggcggcgggg	gtgctgtacg	gaggggacga	tgcccagggc	atgatggcgg	cgatgctgtc	240
ccacgcctac	ggccccggcg	gttgtggggc	ggcggcgccc	gccctgaacg	gggagcaggc	300
ggccctgtc	cggagaaaga	gcgtcaacac	caccgagtgc	gtcccgggtc	ccagctccga	360
gcacgtcgcc	gagatcgtcg	gccgccaggg	ttgtaaaatt	aaagcactga	nagccaagac	420
aaacacgtat	atcaagactc	c				441

&lt;210&gt; 305

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 305

tgcacatgcc	ccctctcttag	cactgcacgg	ccagggtccat	gctgctgcca	cccagacact	60
gggtcttgcc	tgccacactct	gtgggcagag	cttcgaggcg	tggttgggccc	tggtctctga	120
ctctcgggcc	cattcagctc	caaaagcggc	catcgcttgt	cccaaatgcg	agagacgctt	180
ctggcgacga	aagcagcttc	gagctcatct	cgggcggtgc	caacctcccg	cccggaggcg	240
ccggcccttc	atatgcggca	actgtggccc	gagctttgcc	cagtgggacc	agctagtgtc	300
ccacaagcgg	gtgcaactag	ctgaggccct	ggaggaggcc	gcagccaagg	ctctggggcc	360
ccggcccgag	ggcgcccccg	cggtgaccgc	cccccgcccc	ggtggagatg	ccgtcgaccg	420
cccttccag	tgtgcctgtt	gtggcaagcg	cttcggcgac	aagccaact	tgatcgctca	480
cccgcggtg	c					491

&lt;210&gt; 306

&lt;211&gt; 547

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(547)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 306

tctcttctt	ttaagacagc	aatgtaagcc	acaacattta	caaatacaat	gttttaactc	60
totacatgta	ggaagccaac	ctgctccttt	ttgatcttct	tctttggcac	aaacctcagt	120
gatttctctg	attcagaacg	agttctaatt	gatcttctct	gttgcttctt	ttctacttag	180
ccgtgtagaac	cagatgtttg	ttcaggagat	gatacactct	gcgttggtgt	ttcattttct	240
tgttttggtg	tagaaaattat	aagcctgtct	tgccccctga	cacttatttc	tgttttgtta	300
ccaattccct	ttgttgaata	aacaaattga	tcgataaatt	tcccatcccc	tgtagcattc	360
tgaagagc	acaactgttc	aattttcaca	actggagaca	tgttacaact	ctgcaaatcc	420
aggctccctt	tgtgcatccg	taatggaagc	tggttaaggat	ttccttgctg	cccgagtttt	480
ccagctattt	taaacaggcg	ngngctcttc	ctctttccgc	acttggtgtc	cgctcttgcc	540
tatgtctt						547

&lt;210&gt; 307

&lt;211&gt; 571

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(571)  
 <223> n = A,T,C or G

<400> 307  
 cgctgcacgt gataatgtca tcattttatt ttaaatgggt ctaaaattgca natttaagtt 60  
 gatttcaaat caacctatt tttaaattac ttttaaatagg aanaaatgaa gcaaggacat 120  
 acataactca ctatatgtga aggaactcaaa caaatacatg tttggctgtg aattctgtac 180  
 tctcaccaaa acagagataa aaatccacct aaaatacact ttccttcatt tagtgcttgt 240  
 ggganaagggt caagtattgc actttaaaat tactttcact taacatttgc cccaactttc 300  
 cccctgaatt cactatatgt ttccagcaaa catgatttta taaattttaa gtataaaaagc 360  
 aactagggtt tctaattcaa ctttgggaag tttactttac tctacanagc tatttttgta 420  
 aaacggcata tttaacttaca aaattganag ataggggcat ccagctgagg tacatttctc 480  
 cccttggcgt tgagtttctg gacttgggtc gggggcacag gcttgtgtga ctgccccgtg 540  
 gcccgatata tggcctggac cccaggatgc g 571

<210> 308  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(591)  
 <223> n = A,T,C or G

<400> 308  
 ctctctatgt gtctgcctac ttcattcttc ggcatttctc gcttatccaa gttcaccatt 60  
 tcaggtaacc actggtatgc agttgcctgt atataattat caggcatttc ctgcttatcc 120  
 aagttcacca ttccaggtca ccaactggata tcagttgcct gtatataatt atcaggcatt 180  
 tcctgcttat ccaagttcag catttcaggt caccactgga tatcagttgc ctgtatataa 240  
 ttatcaggca ttctctgctt atccaagttc accatttcag gtcaccactg gatatacagt 300  
 gctgtatat aattatcagg catttctctg ttatccaagt tcaccatttc aggtcacacc 360  
 tggatatcag ttgcctgtat ataattatca ggcatttctc gcttatccaa gttcaccatt 420  
 tcaggtaacc actggtatgc agttgcctgt atataattat caggcatttc ctgcttatcc 480  
 aaattcagca gtctcaggtc ccaactggata tcagttccat gtatacaatt accagatgcc 540  
 accgcagtg cctgttgggg gagcaaaagga gaaatntgtg gaccgaagca t 591

<210> 309  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<400> 309  
 aggggggtgca cgtactccca actgtggtcg cgtctctacc ccttctgtgt ctctcgtggc 60  
 cccctcgcca tggcgggcat cctgttttag gatattttcg atgtgaagga tattgaccgc 120  
 gagggcaaga agtttgaccg aggtaaagtaa gtgtctcgac tgcattgtga gagtgaatct 180  
 ttcaaatagg atctaattctt agatgtaaac attcaaatatt accctgtaga cttgggtgac 240  
 aagtttccgt ttggtcatagc tagtaccttg tatgaagatg gtaccctgga tgaatggtgaa 300  
 tacaaccoca ctgatgatag gccttccagg cgtgaccagt ttgagtatgt aatgtatgga 360  
 aaagtgtaca ggattgaggg agatgaaact tctactgaag cagcaacacg cctgctgaga 420  
 ttgagagctg ctgagtgcca gtgctccaga atcacgggat ggggccttct gtttcagctc 480  
 tgcgtacgtg tcttatgggg gctgtctcat gaggctgcag ggggatgcca acaacctgca 540  
 tggattcgag gtggactcca gagtttatct cctgatgaag aagctagctc t 591

<210> 310

<211> 488  
 <212> DNA  
 <213> Homo sapien

<400> 310  
 tgggtctcaag cctgaagagg ctccgcccac aagctggccc atgaagttag caatgcctgt 60  
 ggcttcagtc aattgtcttg agactgtgaa gaggctgaaa gacaccttcc cgggtggaag 120  
 aaggagtcca ctgaaaactt atcttaaaact gaccttccc tttgagttag tcttcattcc 180  
 tctcccatgt gggaaccagc cctccgatgc cccggggact aggggaaaca gttggaggtc 240  
 cgtgcctgcc ccagcctgcc acgggtgcga ggacagccaa gtcctgagt actcaagatg 300  
 cttcacttac atggaagaaa cttctaaaac tctaccgagt ggtttttgta tataactaaag 360  
 ttctatttag agcttttctg ttttgggcaa gttcgctgct ccttctattt gggcactttg 420  
 gttttgttac tgtctttgtg gacggcattg attgaacatt ttttactagt agtcttatga 480  
 cttttgta 488

<210> 311  
 <211> 511  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(511)  
 <223> n = A,T,C or G

<400> 311  
 ccggttntg nagcaaaaaa gggggaagat ttataggtag aggcgacaaa cctaccgagc 60  
 ctggtgatag ctggtgtgcc aagatagaat cttagttaa ctttaaaatt gccacacaga 120  
 ccctctaaat cccttgttaa atttaactgt tagtccaaag aggaacagct ctttgagcac 180  
 taggaaaaaa ccttgtagag agagtaaaaa atttaacacc catagtaggc ctaaaagcag 240  
 ccaccaatta agaaagcggt caagctcaac acccaactacc taaaaaatcc caaacatata 300  
 actgaactcc tcacacccaa ttggaccaat ctatcacctc atagaagaac taatgttagt 360  
 ataagtaaca tgaaaacatt ctctccgca taagcctgcg tcagattaaa acactgaact 420  
 gacaattaac agcccaatat ctacaatcaa ccaacaagtc attattacc tcaactgtcaa 480  
 cccaacacag gcatgtctcat aaggaaaggt t 511

<210> 312  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<400> 312  
 gaacttgcgt tgaagggaagc agaaactgat gaaataaaaa ttttctgga agaaagcaga 60  
 gccacgaga aggagacctt gaaatctctt cttgaacaag agacagaaaa ttgagaaca 120  
 gaaattagta aactcaacca aaagattcag gataataatg aaaattatca ggtgggctta 180  
 gcagagctaa gaactttaat gacaattgaa aaagatcagt gtatttccga gtttaattagt 240  
 agacatgaag aagaatctaa tatacttaaa gctgaattaa acaaagtaac atctttgcat 300  
 aaccaagcat ttgaattaga aaaaaacctt aaagaacaaa taattgaact gcagagtaaa 360  
 ttggattcag aattgagctt ctttgaaga caaaaagatg aaaaattac ccaacaagaa 420  
 gagaataacg aagctattat ccagaacctt gagaagaca gacaaaaatt ggtcagcagc 480  
 caggagcaag acagagaaca gttaattcag aagcttaatt gtgaaaaaga tgaagctatt 540  
 cagactgcc taaaagaatt taaattggag agagaagttg ttgagaaaga g 591

<210> 313  
 <211> 373  
 <212> DNA  
 <213> Homo sapien



<220>  
 <221> misc\_feature  
 <222> (1)...(373)  
 <223> n = A,T,C or G

<400> 313  
 ttgattttta ttctgnattt tattactgaa atangttgtc ctantnatcc caccocacaa 60  
 taaaaatntn acccangccc cccntttctt tncctnatnc cctnttccac cacaccatcc 120  
 cggaacaagt gctccaggat tccctgcccc ctggccattt tggagtgtgn ccattgggta 180  
 gcaatgtgga aaccaccaag ccttttgtgg anaaaaatga gggggtttag ggagnccan 240  
 gaggggctna tttaggggcc ttgtccactt gctcataggc gagctonac tctctntnat 300  
 ctgnacangt ggaagcaaat tcttccgggg cgtnggnant gctnaagnac cgtagcactc 360  
 cccggaaggn ctn 373

<210> 314  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(591)  
 <223> n = A,T,C or G

<400> 314  
 ccgctgcgc cgccgcctcc tgggaagaga ggaagcgga gaggagocca cgtgcctgt 60  
 caccocaatc ctccagccgc gcagtcocga agagtgtaa atgttcgct gcgccaagct 120  
 cgctgcacc cctctctga tccgagctgg atccagagtt gcatacagac caatttctgc 180  
 atcagtgta tctgcaccag aggcctagtag gactggagag ggctctacgg tatttaatgg 240  
 ggcccagaat ggtgtgtctc agctaatacca aaggaggatt cagaccagtg caatcagcag 300  
 agacattgat actgctgcca aatttatgg tgcagggtct gcaacagtag gagggtgctg 360  
 ttctggtgct ggtattggaa cagtctttgg cagccttacc attggttatg ccagaaaccc 420  
 ttgcgtgaag cagcagctgt tctcatatgc tatcctggga ttgctctgt ctgaagctat 480  
 gggtctcttt tgtttgatgg ttgctttctt gattttgttt gccatgtaac aaattactgc 540  
 ttgacatggt ggcattcata taattacng atgtaattct gtgtattctta c 591

<210> 315  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(591)  
 <223> n = A,T,C or G

<400> 315  
 aagcccttca ccaacaaga tgcctatact tgtgcaaat gcagtgcttt tgtccacaaa 60  
 ggctgcagag aaagtctagc ctctctgtga aaggtcaaaa tgaagcagcc caaaggagagc 120  
 cttcaggcac atgacacatc atcactgcc acggctatta tgagaaacaa gccctcacag 180  
 cccaaggagc gtctcgggtc cgcagtcctc ctggtggatg aaaccgctac caccccaata 240  
 ttgtccaata gacgatccca gcagagtgtc togtcttcca aaagtgtctc catacagaac 300  
 attactggag ttggcaatga tgagaacatg tcaaacacct ggaatttct gtctcattca 360  
 acagactcac taaataaaat cagcaaggtc aatgagtcaa cagaatcact tactgatgag 420  
 ggtacagaca tgaatgaagg acaactactg ggagactttg agattgagtc caaacagctg 480  
 gaagcagagt cttggagctg gataatagac agcaagtttc taaaacagcc aaagaaaga 540  
 tgtgggtcaa acngcgagaa gtaatatatg agttggatgc agacagagtt t 591

<210> 316  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<400> 316  
 gttttttataa gaataaaaatt ccattcaagc cagatgggtgt ttacattgaa gaagttctaa 60  
 gtaaatggaa aggaagattat gaaaaactgg agcacacca cacttacatt caatggccttt 120  
 tccccctgag agaacaaggc ttgaacttct atgccaaga actaacata tatgaaattg 180  
 aggaattcaa aaaaacaaaa gaagcaatta gaagattcct cctggcttat aaaatgatgc 240  
 tagaattttt tggaataaaa ctgactgata aaactggaaa tgttgctcgg gctgttaact 300  
 ggcaggaaag atttcgcacat ctgaatgagt ccagcacaa ctatttaaga atcactogta 360  
 ttcttaaaag ccttggtgag cttggatatg aaagttttaa atctcctctt gtaaaattta 420  
 ttcttcatag agctcttggt gagaatacta ttcccaatat taagcagagt gctctagagt 480  
 attttggttt tacaattaga gacagaagag aaaggagaaa gctcctgctg ttgcgccaga 540  
 aacactacac gccttcagag aactttatct ggggacccgc ctcgaaaaa a 591

<210> 317  
 <211> 323  
 <212> DNA  
 <213> Homo sapien

<400> 317  
 ccaagctacg gaagcaagtg gaagagattt ttaatttgaa atttgcctaa gctcctggac 60  
 tcaccaggcg agtaaaaagta ccatatcctg tgtttgaatc aaacccggag ttctctatg 120  
 tggaaagcct gccagagggg attcccttcc gaagccctac ctgggttgga attccacgac 180  
 ttgaaaaggt cgtccacggg agtaataaaa tcaagttcgt tgttaaaaaa cctgaactag 240  
 ttatttctta ctgtcctcct gggatggcta gtaaaataa cactaaagct ttgcagctcc 300  
 ccaaagacc acgaagtcct ggg 323

<210> 318  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(591)  
 <223> n = A,T,C or G

<400> 318  
 gatggcgtag ttggccttggaa gactggcgcg cggcttcgtgt ccgagttctc tgcaggtcac 60  
 tagtttcccg gtagttcagc tgcacatgaa tagaacagca atgagagcca gtcagaagga 120  
 ctttgaaaat tcaatgaatc aagtgaacct cttgaaaaag gatccaggaa acgaagtga 180  
 gctaaaaact tacgcgctat ataagcaggc cactgaagga ccttgtaaca tgcccaaac 240  
 aggtgtattt gacttgatca acaaggccaa atgggaagca tggaaatgcc ttggcagcct 300  
 gcccaaggaa gctgccaggc agaactatgt ggatttgggt tcagtttga gtccttcatt 360  
 ggaatcctct agtcaggtgg agcctggaac agacaggaaa tcaactgggt ttgaaactct 420  
 ggtgggtgacc tccgaagatg gatccacaaa gatcatgttc aacgggccca aaaaagaaaa 480  
 tgccataaac actgagatgt atcatgaaat tatgctgtca cttaaagctg ccagcaanga 540  
 tgactcaatc atcactgttt ttaacaggaa atggtgacta ttacagtagn g 591

<210> 319  
 <211> 591  
 <212> DNA  
 <213> Homo sapien

<400> 319

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gaattcggca cgaggttgct gctaagcgaa cgccctttgg agcttacgga ggccttctga      60
aagacttcac tgctactgac ttgtctgaat ttgctgccaa ggctgccttg tctgtcggca      120
aagtctcacc tgaacaggtt gacagtgatg ttatgggcaa tgcctgcag agttcttcag      180
atgctatata ttggcaaggt catgttggtt tgcgtgtggg aatcccaaaag gagaccccaag      240
ctctcacgat taatagagct tgtggttctg gttttcagtc cattgtgaat ggaatgtcagg      300
aaatttgggt taaagaagct gaagttgttt tatgtggagg aaccgaaagc atgagccaag      360
ctccctactg tgtcagaaat gtgcgttttg gaaccaagct tggatcagat atcaagctgg      420
aagattcttt atgggtatca ttaacagatc agcatgtcca gctccccatg gcaatgactg      480
cagagaatct tgctgtaaaa cacaaaataa gcagagaaga atgtgacaaa tatgcctctg      540
agtccacaga gagatggaaa gctgctaatt atgctgggcta cttaatatga g      591

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&lt;210&gt; 320

&lt;211&gt; 591

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(591)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 320

```

ggctccggcg tctgcagggg tcgcgcagct aaccctgggc taggcgagtg gggcggggcg      60
ggcggcaccg tgctcgaggca ggcgaaccgt ggcaccgaga gcaagaaaat gagctctgag      120
ctcttcaccc tgacctatgg tgccctgggt acccagctat gtaaggacta tgaaaaatgat      180
gaagatgtga ataaacagct ggacaaaatg ggctttaaca ttggagtccg gctgattgaa      240
gatttcttgg ctccggtcaa ttgtgggagg tgccatgact ttccgggaaac tgcggatgtc      300
attgccaaag tggcgttcaa gatgtacttg ggcatactc caagcattac taattggagc      360
ccagctgggt atgaattctc cctcattttg gaaaataacc ccttggtgga ctttggtgaa      420
cttctgata accactcatc ccttatttat tccaatctct tgtgtggggt gttgcgggga      480
gctttggaga tgggtccagat ggtcngngga ggcccaagtt tgtccaggac accctnaaag      540
gagacggngg tgacagaaat ccgcatgaga ttcactcagg ggattganga c      591

```

&lt;210&gt; 321

&lt;211&gt; 260

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(260)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 321

```

ctgcttggtc ccacacgtgg gccgcgtag gtattccgac cggaattcc tcctattggt      60
gtgcagcagc cacattgaag gatagagtgg cagcagaggc caaggatcgt gagtgtatgg      120
agtttgtctg tgaaaatgaa ggggaagtct ggggaggtct ccacagcgtg gctgaggggg      180
tgccgctaag tccagagcct ggcagggagg gagtaaggga cttagcaggg gcggaggagg      240
tctgcgnggg anaggagggg

```

&lt;210&gt; 322

&lt;211&gt; 559

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(559)

<223> n = A, T, C or G

<400> 322

ttccacatga	catggagtggt	gaagctggat	gagcacatca	ttccactggg	aagcatggca	60
nttaacagca	tctcaaaact	gactnancct	accagctctt	ccatgtattc	acttctaat	120
gcaccacact	tggcanacct	gnaggacnat	acacatgaag	ncantgatga	tcagccagan	180
aanctcact	ttgactctcg	canngtgata	tttgagctgg	attcatgcaa	tggagtgagg	240
aaagtgttgc	ttgtctacaa	aagtgggaaa	ccagnattag	cagaanacac	tgagatctgg	300
ttcctgnaca	nancgttata	ctggcatttt	ctcacanaca	cctttactgc	ctattaccgc	360
ctgctcatca	cccactcggg	cctgcccag	tggaatatg	ccttccagc	tatggcatta	420
gcccacaggg	caagcaatgg	ttcagcatgt	ataaacctat	cacctacaac	acaaacctgc	480
tcacagaaga	naccgactcc	tttgtgaata	agctagatcc	canctnagtg	tttaagagca	540
agaacaagat	cggtatccc					559

<210> 323

<211> 492

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(492)

<223> n = A, T, C or G

<400> 323

cctgtctccc	agccgtacca	gagagggtc	ggccggcagc	gccgggctgg	ggggcgccgg	60
cgccggcgcc	ggagccgggg	tgggtgcagg	cgccggcggg	ggcagcgccg	cgagcagcgg	120
cgccggggcc	ggggggctgc	aaccacagcag	ccgcgctggc	ggcgccggcc	cctccagccc	180
cagcccgctg	gtggtagagc	agaaggagaa	ggaagagtgt	gagcgctgcg	agaaagagga	240
ggaggagagg	aagaagaggg	tgacagctga	tgtgttcgtg	atgcgctgca	tcgcctaccc	300
ctttaatgcc	aagcagccca	ccgacatggc	tgcggcgagc	cagaagatca	gcaaacagca	360
gctgcagaca	gtcaaggacc	ggtttcaggc	tttctcfaat	ggggaaaccc	anacatggc	420
tgacgaagcc	ttcatgaacc	gctgtngcag	agttactatg	aggtgttctc	gaagaccacc	480
cgtgtggccg	ca					492

<210> 324

<211> 474

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(474)

<223> n = A, T, C or G

<400> 324

aatttcagca	acatacttct	caattttctc	aggatttaaa	atcttgaggg	attgatctcg	60
cctcatgaca	gcaaggtcga	tggttttgcc	acctgactga	accacttcca	ggagtgccct	120
gatcaccagc	ttaatgtgtca	natcatctgt	ttcaatggct	tcgtcagtat	agttcttctc	180
cagnaactca	cgcactgact	tggcaccgcc	gcctatggca	ttggccttcc	aggcatggta	240
tggtcccgag	gggtcagctc	gatagagcct	aggagtgcga	tcaaatgtga	aacccacgat	300
gagggcagat	atgccaaaag	gcctgcgcc	attgctctcg	gtataacgct	gcttcanact	360
ggcgatgtag	cggtgatgt	actccacagt	gaccgggtcc	tcacacgtca	ggcggtggct	420
ctggcactcc	accgcggccc	tggtgatgac	tatecttgca	tcggcggtga	ggcc	474

<210> 325

<211> 532

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(532)

<223> n = A,T,C or G

<400> 325

gaggagacag	gacagagcgt	ctggagaggc	aggaggacac	cgagttcccc	gtgttgccct	60
ccaggtccctg	tgcttgcgga	gccgtccggc	ggctgggata	gagccccgac	aatgggcaac	120
gcgcaggagc	ggccgtcaga	gactatcgac	cgcgagcgga	aacgcctggt	cgagacgctg	180
caggcggaact	cgggactgct	gttggacgcg	ctgctggcgc	ggggcgtgct	cacggggcca	240
gagtagcgagg	cattggatgc	actgcctgat	gccgagcgca	gggtgcgcgc	cctactgctg	300
ctgggtgcagg	gcaagggcga	ggccgcctgc	caggagctgc	tacgctgtgc	ccagcgtaacc	360
cggggcgcgc	cggacccgcg	ttgggactgg	cagcacgtgg	gtccgggcta	ccgggaccgc	420
agctatgaacc	ctccatgcc	aggccactgg	acgcccggagg	caccgggctc	ggggaccaca	480
tgccccgggt	tgcccagact	tcagaccctg	acgagmcgg	ggggccctgag	gg	532

<210> 326

<211> 322

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(322)

<223> n = A,T,C or G

<400> 326

caaaattaac	atttttatta	aatcaagtta	aaaaaaaaatgt	tcagtgtana	aaagtcaaca	60
aggggttttaa	caaaaccaaa	atataccttt	ttatacaata	tatgtatata	ttagcagcaa	120
actacttctgt	anattctctt	tcttttatgt	tcttctagtt	attttaaaga	aagcataaac	180
aatgtatatatt	agtatggaat	gtcagcaaat	ccactcttag	tcctttatct	tgtgattttg	240
gccttctaca	aaatactttg	tgattctcac	taatgaataa	taagaacata	cccaatttta	300
actaaaaagt	agtgaacag	tg				322

<210> 327

<211> 387

<212> DNA

<213> Homo sapien

<400> 327

aaaaaccgtgt	actattagcc	atggtcaacc	ccaccgtgtt	cttcgacatt	gccgtcgagc	60
gcgagccctt	ggccgcgctc	tcctttgagc	tgttttgcaga	caaggtccca	aagacagcag	120
aaaatttttcg	tgctctgagc	actggagaga	aaggatttgg	ttataagggt	tcctgctttc	180
acagaattat	tcacgggttt	atgtgtcagg	gtggtagact	cacacgccat	aatggcactg	240
gtggcaagtc	catctatggg	gagaaatttg	aagatgagaa	cttcattccta	aagcatacgg	300
gtcctgcat	cttgtccatg	gcaaatgctg	gacccaacac	aaatggttcc	cagtttttca	360
tctgcactgc	caagactgag	tggttg				387

<210> 328

<211> 502

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(502)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 328

agcagcccg	cgccgccc	gcgcgcgcgc	gcggcaagcg	tccgggcccag	catgggggct	60
tcgtggtgac	tgctcaagcaa	gagcgcgcg	aggggtccacg	cgcgggcgag	aagggggtccc	120
acgaggagga	gcccgtgaag	aaacgcggct	ggcccaagg	caagaagcgg	aagaagattc	180
tgccgaatgg	gcccgaaggca	ccgggtcacg	gctacgtgcg	cttctgaac	gagcgcgcg	240
agcagatccg	cacgcgccac	ccggatctgc	cctttcccga	gatcaccaag	atgctggg	300
ccgagtgag	caagctgcag	ccaacggaaa	agcagcggt	cctggatgag	gccnagagag	360
agaagcagca	gtacatgaag	gagctgcgg	cgtaccagca	gtctgaagcc	tataagatgt	420
gcacggagaa	gatccaggag	aagaagatca	agaaagaaga	ctcgagctct	gggctcatga	480
acactcttct	gaatggacac	aa				502

&lt;210&gt; 329

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(463)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 329

caagttgcac	attttaattt	acaattttta	ccaataaaaa	ggattagttt	acaaaaagg	60
aagtccttta	tacaaaaata	ggacaatttg	taaaganaat	ccactgtcat	gttttgctt	120
gtcaagtcaa	aactcaata	gcttggtttg	gtaaaaattat	tccagaaaca	taatccagac	180
aaaatcaata	acgtcatcag	cttcctaacc	atgtttaana	ggaataactt	catgaacatt	240
ttgcctgaa	ctgaanagtt	ctaaataactt	gtaaaccttt	agggaaaaat	gactgtctgc	300
agggcagctt	actggttaaga	gggtacacca	nagactccg	gtcactcact	gtcagaatat	360
tctttatacat	acaatgagtc	tccacgcctg	tacaatgagt	gtcgtgcac	ataattggag	420
taatggcctc	taaaatttta	caagtaaaact	ttattnggc	ccc		463

&lt;210&gt; 330

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(500)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 330

taattataga	tctacaaaat	atgaaatgta	ttccaagaat	gcagaaaaac	catctagaag	60
caaaaggact	ataaaacaaa	aacagagaag	aaaattcatg	gctaaccag	ctgaagaaca	120
gcttggtgtg	ggacagctcta	aagatgaaaa	catacataca	tcacatatatta	cccaagacga	180
atttcaaaga	aattcagaca	gaaatatgga	agagcatgaa	gagatgggaa	atgattgtgt	240
ttccaaaaaa	acagatgcc	cctgtgggaa	gcaagaaaa	tagcactaga	aaagataagg	300
aagaatctaa	aaagaagcgc	ttttccagtg	agtcacagaa	caaaactgtg	cctgaagaag	360
tgacttcaac	tgctcacgaaa	agtcgaanaa	tttccangcg	tccatctgat	tggtgggtgg	420
taaaancaga	ggagagtcct	gtttatagca	atttctcagt	aagaaatgaa	ttaccaantg	480
catcacaaatn	ntgcccgga					500

&lt;210&gt; 331

&lt;211&gt; 494

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(494)  
 <223> n = A,T,C or G

<400> 331  
 tctctctctc tctcaaaatt acagtgttca ttgtcattga cctcagcagc aaatttgact 60  
 tgaatttcact taggatcgca ggaatcaggg gaaagtgtt ttaaagggtg tttctccagc 120  
 acattttaag aaaaagggacc aaaagttatt ttagcttcct caatagattg catgttgctt 180  
 attaggataa taaattaata ttaaatgcaa tatatgtctt gnotttatta tggcactctat 240  
 ttaggagttg ttcaaatcac tgcagtaggg ctctgcaaat aaaataatgn aaactattat 300  
 catggatcta atgnactgna actttatcag tgaagggnaa aatctcaaat aacaagtaca 360  
 aacattggac aattacctat aaagatttgt aaaagaaaa' tttttccata gattttcattc 420  
 ttggcatttt gtaaaagaca ccttcgcagc cctctgttgn aactttttta ataaaataga 480  
 catctgttta cttg 494

<210> 332  
 <211> 538  
 <212> DNA  
 <213> Homo sapien

<400> 332  
 aaagaacaaa tgggaacgca tgggtgttct gaacaagagt ctcaaccgtg tgcatttatt 60  
 gggataggaa atagtggacca agaaatgcag cagctaaact tgggaaggaaa gaactattgc 120  
 acagccaaaa cattgtatat atctgactca gacaagcgaa agcacttcatt gttgtctgta 180  
 aagatgttct atggcaacag tgatgacatt ggtgtgttcc tcagcaagcg gatataaagtc 240  
 atctccaaac cttccaaaaa gaagcagtc tttgaaaaatg ctgacttatg cattgcctca 300  
 ggaacaaagg tggctctgtt taatcgacta cgatcccgaa cagtttagtac cagatacttg 360  
 catgtagaag gaggtaatctt tcatgccagt tcacagcagt ggggagcctt ttttattcat 420  
 ctcttgatg atgatgaatc agaaggagaa gaatttcacag tccgagatgg ctacatccat 480  
 tatggacaaa cagtcaaaact tgtgtgctca gttactggca tggcactccc aagattga 538

<210> 333  
 <211> 499  
 <212> DNA  
 <213> Homo sapien

<400> 333  
 ctcagcctgc gggactgcctc ggctcggctt ctaggcggtt ttgatgaaca cctggcttta 60  
 tctttgcaat gaagaaagggt tctcaacaaa aaatattctc caaagcaag ataccatcat 120  
 catctcactc tccatcccca tcatctatgt ccaatatgag atctaggta ctttcaacct 180  
 tgattggatc agagactcta ccttttcatt ctggaggaca gtggtgtgag caagttgaga 240  
 ttgcagatga aaacaatatg cttttggact atcaagacca taaaggagct gattcacatg 300  
 caggagttag atataattaca gaggccttca ttaaaaaact tactaaacag gataatttgg 360  
 ctttgataaa atctctgaac ctttccactt ctaaagcagg tggcaagaaa ttttaagtata 420  
 ttgagaattt ggaaaaattg gttaaaactt aagtactgaa tctcagctat aatctaatag 480  
 ggaagattga aaagtcgga 499

<210> 334  
 <211> 561  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(561)  
 <223> n = A,T,C or G

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<400> 334
ttcccggtag ttcagctgca catgaataga acagcaatga gagccagtca gaaggacttt 60
gaaaattcaa tgaatcaagt gaaactcttg aaaaaggatc caggaaacga agtgaagcta 120
aaactctacg cgctatataa gcaggccact gaaggacctt gtaacatgac caaacccagg 180
gtatttgact tgatcaacaa ggccaaatgg gacgcgatga atgcccttgg cagcctgccc 240
aaggaaagctg ccaggcgaga ctatgtggat ttgggtgtcca gtttgatgcc ttcatgtgaa 300
tcctctagtc aggtggagcc tggaacagac aggaatcaa ctgggtttga aactctgggtg 360
gtgacctccg aagatggcat cacaagatc atgttcaacc cggcccaaaa agaaaatgc 420
cataaacact gagatgtatc atgaaattat gcgtgcactt aaagctgcca gcaaggatga 480
ctcaatcatc actgttttaa cangaaatgg tgactattac agtagtgga atgatctgac 540
taacttctct gatattcccc c 551

```

<210> 335

<211> 551

<212> DNA

<213> Homo sapien,

```

<400> 335
aagctgggtca tggctgggga gaccaccaac tcccgcggcc agcggctgcc ccagaaggga 60
gacgtggaga tgctgtgccc cgggccgccc tgccagggct tcagcggcat gaaccgcttc 120
aattcgcgca cctactccaa gtccaaaaac tctctgggtg tttccttctc cagctaactg 180
gactactacc ggcccgggtt ctctctctcg gagaatgtca ggaactttgt ctccctcaag 240
cgctccatgg tcttgaagct caccctccgc tgctctgtcc gcatgggcta tcagtgcacc 300
ttcgcgctgc tgcagcgccg tcagtagcgc ctggcccaga ctaggaggcg gcccattcatc 360
ctggccgccc cccctggaga gaagctccct ctgttcccg agccactgca cgtgtttgct 420
ccccggccct gccagctgag cgtggtgggt ggatgacaag aagtttgtga gcaacataac 480
caggttgagc tcgggtctct tccggacct acggtgcgag aaacgatgtc cgacctgccg 540
gaagtgcgga a 551

```

<210> 336

<211> 540

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(540)

<223> n = A,T,C or G

```

<400> 336
aggtctatgt ctactgaag caataaacga ggaatgatcc agcttattgt tgcaaggaga 60
ataagcaagt gcaatgagct gaagtcacct gggagccccc ctggacctga gctgccatt 120
gaaacagcgt tggatgatag agaacgaaga atttccatt cctctaacag tgggattgag 180
gggcttgatg aatgcgccag cagaaatgct gccctcagta ggataatggg taaataccag 240
ctgtccccta cagtgaatat gccccaagat gacactgtca ttatagaaga tgacaggttg 300
ccagtgtctt ctccacatct ctctgaccag tctcttcca gctcccatga tgatgtgggg 360
tttgtgacg cagatgctga taactgggcc aaggctgcaa tcagtgtatc agccgactgc 420
tccttgagtc cagatgttga tccagttctt gcttttcaac gaaaaaggat ttggacgtca 480
gaagtatgtc agaaaaacgc accaaagcaa ttttcanatg ccagtcaatt ggatttcggt 540

```

<210> 337

<211> 422

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature



&lt;222&gt; (1)...(422)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 337

gcagcaggaa	cagttacagc	agcagcagca	acagcagctg	ttgcaacagc	agcaggaaaca	60
atttgcagcag	caacaactgc	agcctcctcc	cctggagccc	gaggaggagg	aagaggtgga	120
gctggagctc	atgcgcgttg	acctgggggtc	agagcaggag	ctggagcagc	agcggcaggga	180
gttggagcgg	cagcaggagc	tggaaacggca	gcaggagcag	cggcagctgc	agctcaaaact	240
gcaggaggag	ctgcagcagc	tggagcaaca	gctggagcag	cagcagcagc	agctggagca	300
gcaggagggtg	cagctggagc	tgaccccggt	ggagctaggc	gcccagcagc	aggaggtgca	360
gctggagctg	acccccgtgc	agccggagct	gcagctggaa	ctggtgccan	cccagggggc	420
gg						422

&lt;210&gt; 338

&lt;211&gt; 601

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(601)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 338

catcttaaga	acgctctatg	atgtcttatg	agcggctctat	gatgtcccct	atggctgaac	60
gctctatgat	gtcagcctac	gagcgcctcta	tgatgtcagc	ctacgagcgc	tcctatgatgt	120
ccccctatggc	tgagcgcctct	atgatgtcag	cttatgaacg	ctccatgatg	tcagcttatg	180
aacgctccat	gatgtcccca	atggctgatc	gatctatgat	gtccatgggt	gctgaccgggt	240
ctatgatgtc	gtcactactct	gctgctgacc	ggtctatgat	gtcatogtat	tcctgcagctg	300
acgatctat	gatgtcactt	tatactgctg	atcggtcaat	gatgtctatg	gctgtgatt	360
cttacaccca	ttcttacaact	gacacatata	cagaggcata	tatggtgcca	ccctttgcctc	420
ctgaagagcc	cccaacaatg	ccaccgttgc	cacctgagga	gccaccaatg	acaccacat	480
tgctctnctga	ggaaccaccc	agaggggtcca	gcattgccca	cttgagcagt	cagcattaaac	540
cagcttgaag	atacttggcc	ctacanangg	tgccatcatt	accatctgaa	gagctgtatc	600
g						601

&lt;210&gt; 339

&lt;211&gt; 440

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(440)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 339

agaggaggga	ggcccaactg	gtgatgctgc	tgctgctgct	gctgccgcgc	ccgccgcctc	60
tattgctgat	actctagtgg	ggctggaagg	gtggttcta	ttcgaccat	cgccaaaccag	120
agacagaggg	aaaaaaaaaa	ccggcagcca	ctgctgatgt	tgggttcgga	ggctgcatcc	180
gactcggtgc	caagggaact	ggattcagtt	tgcactctc	cctcctttaa	acagcttctc	240
cggtgtctcag	catggtatca	aagcttgaag	gagagaagac	tcaagaagcg	aagaggattc	300
gtgagctgga	gcagcgcaag	cacacggtgc	tgggtgacaga	actcaagcc	aagctccatg	360
aggagaagat	gaaggagctg	caggctgtga	gggagaacct	tatcaagcag	cagcagaggga	420
aatgtcaang	acgtggaagg					440

&lt;210&gt; 340

&lt;211&gt; 450

<212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(450)  
 <223> n = A,T,C or G

<400> 340  
 gatttcacagg ggcggatatt gagtgtcgac ccagaggaag aaagggagga gggcccgcct 60  
 aggatttcctc aggcgcacca gtggaagtct tcaacaaga gcctgggtga ggctctgggg 120  
 ctgggaagccg aggggtcgagt tcttgagaca cagactttga cgggatggag taaggggttc 180  
 attggcatgc acagggaaat gcaagtcaac cccatttcaa agcggatggg gcccatgact 240  
 gtggtcagga tggacgcttc agtccagcca ggcccttttc ggaccctgct ccagtttctt 300  
 tatacgggac aactggatga aaaggaaaag gatttggtgg gcctgggtca gatcgagag 360  
 gtcttcgaga tgttcgattt gaggatgatg gtggaaaaca tcatgaacaa ggaagccttc 420  
 atgaaccagg agattacgaa nncctttcac 450

<210> 341  
 <211> 451  
 <212> DNA  
 <213> Homo sapien

<400> 341  
 aacagctatt aaaacagaaa atggatgaac ttcataagaa gttgcatcag gtggtggaga 60  
 catcccatga ggatctgccc gcttcccagg aaaggtccga ggttaatcca gcacgtatgg 120  
 ggccaaagtgt aggtctccag caggaactga gagcgccatg tcttccagta acctatcagc 180  
 agacaccagt gaacatggaa aagaacccaa gagaggcacc tctctgtgtt cctcctttgc 240  
 caaatgctat tctgcagct ttggtgtccc cagccaccag coagagcatt gctcctcttg 300  
 ttcttttgaa agcccagaca gtaacagact ccatgtttgc agtggccagc aaagatgctg 360  
 gatgtgtgaa taagagtact catgaattca agccacagag tggagcagag atcaagaag 420  
 ggtgtgaaac acataagggt gccaacacaa g 451

<210> 342  
 <211> 498  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(498)  
 <223> n = A,T,C or G

<400> 342  
 ctcaagcagg ctattgaaga ggaaggaggc gatccagata atattgaatt aactgtttca 60  
 actgatactc caaacaagaa accaactaaa ggcaaaagta aaaaacatga agcagatgag 120  
 ttgagtggag atgcttctgt gggaagatga tgcttttctc aaggactgtg aattggagaa 180  
 tcaagaggca catgagcaag atggaaatga tgaactaaag gactctgaag aatttgggtg 240  
 aaatgaagaa gaaaatgtgc attccaagga gttactctct gcagaagaaa acaagagagc 300  
 tcatgaatta atagaggcag aaggaataga tacatataga aaagaggaca tcgaaagta 360  
 ggaaattgaa gctcaagaag gtgaagatga tacctttcta acagcccaag atggtgagga 420  
 agaagaaaat gagaagata tagcagggtt ctggtgatgg cncacaagaa gatatnaaac 480  
 ctcttccttc aaaaaggg 498

<210> 343  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

```

<400> 343
ccgaccacct ctcggcgggc caactccaca accagtagcg ccccatgaat atgaacatgg      60
gtatgaacct ggcagcagcg gcggcccacc accaccacca ccaccaccac cacccccggg      120
cctttttccg ctatatcgcg cagcagtgca tcaagcagga gctaattctg aagtggatcg      180
accccgagca actgagcaat cccaagaaga gctgcaacaa aactttcagc accatgcacg      240
agctggtgac acacgtctcg gtggagcagc tcggcgggcc ggagcagagc aaccacgtct      300
gcttctggga ggagtgctcg cgcgagggca agcccttcaa ggccaaatag aaactgggtca      360
accacatccg cgtgcacaca ggcgagaaac ccttccctgc ccttccgggt gtggcgaagt      420
cttcgcgcgc tccgagaacc tcaagatcca caaagagacc acacagggga gaagccgtcc      480
agtggagttg a

```

```

<210> 344
<211> 412
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(412)
<223> n = A,T,C or G

```

```

<400> 344
gtgcgctgtc ttcccgcttg cgtcagggac ctgcccgcact cagtggccgc catggcatca      60
gatgaaggca aactttttgt tggagggcgt agtttttgaca ccaatgagca gtcgctggag      120
cagggtcttc caaagtagcg acagatctct gaagtgggtg ttgtgaaga caggggagcc      180
cagaagatctc ggggatttgg tttgttcacc ttgagaaca ttgacgacgc taaggatgcc      240
atgatggcca tgaatgggaa gtctgtagat ggacggcaga tccagtagta ccaggcaggc      300
aagtcgtcan acaaccgatc cgtgggttac cgtgggtgct ctgcccgggg ccggggcttc      360
ttccgtgggg gcccgangac ggggcccgtg ggttctctaa aagaagaggg ga      412

```

```

<210> 345
<211> 498
<212> DNA
<213> Homo sapien

```

```

<400> 345
aactagtctc gggccatcct ttctgcgcac ccggtgtcgc tgggctgcac cccggggcgg      60
gacgtccgcg gggcaccgga gggggccaag atgccgatca ataatcaga gaagccagaa      120
agctgcgata atgtgaaggt tgttgtagg tgccggcccc tcaatgagag agagaaatca      180
atgtgctaca aacaggctgt cagtgtggat gagatgaggg gaactatcac tgtacataag      240
actgattctt ccaatgaacc tccaaagaca ttacttttg atactgtttt tggaccagag      300
agtaaaacac ttgattgtta taacttaact gcaagacctt ttattgatto tgtacttgaa      360
ggctacaatg ggactatttt tgcatatgga caaacggaa caggcaaaac ttttaccatg      420
gaaaggtgtc gagctatttc tgaacttaga ggaataattc cccaatttct ttgctcacia      480
tatttgggcc atattttgc

```

```

<210> 346
<211> 427
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(427)
<223> n = A,T,C or G

```

```

<400> 346

```

agatggcgg	cgccgtgaga	actttgcagg	aacagctgga	aaaggccaaa	gagagtctta	60
agaacgtgga	tgagaacatt	cgcaagctca	ccggggcggga	tccgaatgac	gtgaggccca	120
tccaagccag	atttctggcc	ctttctggtc	ctgggtggagg	tagaggacgt	ggtagtttat	180
tactgaggcg	tggattctca	gatagtggag	gaggaccccc	agccaaacag	agagaccttg	240
aaagggcag	cagtaggctg	ggcggggagc	gtcggaccga	aagagaatca	cgccaggaaa	300
gcgaccggga	ggatgatgat	gttaaaaagc	cagcattgca	gtcttcannt	gtagctacct	360
cccaaaagac	gccccacgta	gagaccttat	ccagggatca	aaatttttga	tgaaaagg	420
gaaagcc						427

<210> 347  
 <211> 280  
 <212> DNA  
 <213> Homo sapien

<400> 347						
cacagaaaagt	tctcgcgtcc	cagacatggg	tccctcggtc	tccgtcctcg	gaagcgcagc	60
acgagggcatc	gtgggaaggt	gaagagcttc	cctaaggatg	accggtccaa	gccggtccac	120
ctcacagcct	tctctgggata	caagcgtggc	atgactcaca	tcgtgcggga	agtgcacagg	180
ccgggatcca	aggtgaacaa	gaaggaggtg	gtggaggtcg	tgaccattgt	agagacacca	240
cccatgggtg	ttgtgggcat	tgtgggctac	gtggaaaccc			280

<210> 348  
 <211> 411  
 <212> DNA  
 <213> Homo sapien

<400> 348						
caactatgat	gtgcctgaaa	aatgggcacg	attctatact	gcagaagtag	ttcttgcatt	60
ggatgcaatc	cattccatgg	gttttattca	cagagatgtg	aagcctgata	acatgctgct	120
ggataaatct	ggacatttga	agtttagcaga	ttttgttact	tgtatgaaga	tgaataagga	180
agggcatgta	cgatgtgata	cagcgggttg	aacacctgat	tatatttccc	ctgaagtatt	240
aaaatcccaa	ggtgtgtgat	gttattatgg	aagagaatgt	gactgtgtgt	cggttgggtg	300
atttttatac	gaaatgcttg	taggtgatgc	acctttttat	gcagattctt	tgtgtggaac	360
ttacagtaaa	attatgaacc	attaaaaatt	cacttacctt	tcctgatgat	a	411

<210> 349  
 <211> 408  
 <212> DNA  
 <213> Homo sapien

<400> 349						
gatgggcaatc	tctcgggaga	actggcacaa	gcgcccga	accgggggca	agagaaagcc	60
ctaccacaag	aagcgaaggt	atgagttggg	gcgcccagct	gccaaacacca	agattggccc	120
ccgcgcgcatc	cacacagtc	gtgtgcgggg	aggttaacaag	aaataccgtg	ccctgaggtt	180
ggacgtgggg	aattttctct	ggggctcaga	gtgtttgtact	cgtaaaacaa	ggatcatcga	240
ttgtgtctac	aatgcattcta	ataacgagct	ggttctgtacc	aagaccctgg	tgaagaattg	300
catcgtctctc	atcgacagca	caccgtaccg	acagttggta	gagtcacct	atgcgctgcc	360
cctggggcgc	aagaaggagg	ccaaactgac	ttctgaggaa	gaagaaaa		408

<210> 350  
 <211> 409  
 <212> DNA  
 <213> Homo sapien

<400> 350						
ggttccccca	gctctgggta	cccggtctctg	catcgcgtcg	ccatgatggg	ccatcgtcca	60
gtgctcgtgc	tcagccagaa	cacaaagcgt	gaatccggaa	gaaaagtcca	atctggaaac	120
atcaatgctg	ccaagcatat	tgcagatatc	atccgaacat	gtttggggacc	caagtcacatg	180

atgaagatgc	ttttggacc	aatgggaggc	attgtgatga	ccaatgatgg	caatgccatt	240
cttcgagaga	ttcaagtcca	gcattccagc	gccaaagtcca	tgatcgaaat	tagccgggacc	300
caggatgaag	aggttgagga	tgggaccaca	tcagtaatta	ttcttgcagg	ggaaatgctg	360
tctgtagctg	agcacttctc	ggagcagcag	atgcacccaa	caggtgggg		409

<210> 351  
 <211> 226  
 <212> DNA  
 <213> Homo sapien

<400> 351						
aatcccaaac	atataactga	atcctcaca	cccaattgga	ccaatctatc	accctataga	60
agaaactaatg	ttagtataag	taacatgaaa	acatttctct	ccgcataaagc	ctgcgtcaga	120
ttaaaacact	gaactgcaca	ttacagcccc	aatatctaca	atcaaccaac	aagtcattat	180
taccctcact	gtcaacccaa	cacaggcatg	ctcataagga	aaggtt		226

<210> 352  
 <211> 410  
 <212> DNA  
 <213> Homo sapien

<400> 352						
gcggaggggc	tggctgggca	ggagggggtg	gcgggggcgc	agggccgcgg	ccatggggag	60
cttgaaaggag	gagctgctca	aagccatctg	gcacgccttc	accgcactcg	accaggacca	120
cagcggaag	gtctccaagt	cccagctcaa	ggctccttcc	cataacctgt	gcaagggtgt	180
gaaggttctc	catgaccag	ttgccttga	agagcacttc	agggatgatg	atgaggggtc	240
agtgtccaac	cagggtctaca	tgccttat	aaacagggtc	attttggaaa	aggtccaaga	300
caactttgac	aagattgaat	tcaataggat	gtgttggacc	ctctgtgtca	aaaaaaacct	360
cacaagaagt	ccctgtctca	ttacagaaga	agatgcattt	aaaatatggg		410

<210> 353  
 <211> 380  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(380)  
 <223> n = A,T,C or G

<400> 353						
gagtttattt	agaaagtatc	atagtgtaaa	caaacaaatt	gtaccacttt	gattttctttg	60
gaatacaaga	ctcgtgatgc	aaagctgaag	ttgtgtgtac	aagactcttg	acagttgtgc	120
ttctctagga	ggntgggttt	ttttaaaaaa	agaattatct	gngaaccata	cgtgattaat	180
aaagatttcc	tttaaggcan	aggctggtcn	agatgctgct	gttatcttct	gcctcagaca	240
gacagtataa	gnggtcttgt	ttctaagatt	cctaccacca	gttacttttg	gccaaagtatc	300
cacatccctc	tgcgtatggg	aggnnggtga	anagtgttgg	atgcaaaang	gttattatgg	360
gaagnagctc	natggtataa					380

<210> 354  
 <211> 379  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(379)  
 <223> n = A,T,C or G

```

<400> 354
caacacatct ttattaaaca cctgaagtta ctggaggagg gccatgatgc tggcacacact      60
gtcaaaagtc atcttctcca caatgttctt gggtttaagt ctctcttctt ggctacagaa      120
gaanattctgc cccgactnrg cggcactcca gccgtatttg ctcatccaca ccttagactg      180
gctgtccgac agancccgga gcatntcggc cagcagccan cggnaaatgt gctggtaagt      240
gatacccaca acatggcaga taaacttttc gacanagtct tcaaaaggcc ttataccctc      300
caagaggtcc atgttttcat ccagggcttg ccanaagcct ggaaatggca ggtctccaac      360
aggcccccca ggtacaaaaa

```

```

<210> 355
<211> 499
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(499)
<223> n = A,T,C or G

```

```

<400> 355
gtccagagct gctggtgctc ccgttcccca gacctaccce ctatcccag tggagccgga      60
gtgcggggcgc gccccaccac cgcctcacc atggtgctgt tggcagcagc ggtctgcaca      120
aaagcaggaa aggtctattgt ttctcgacag tttgtggaaa tgaccgcgaa tcggattgag      180
ggcttattag cagcttttcc aaagctcatg aacactggaa acaacatac gtttgttgaa      240
acagagatgc taagatatgt ctaccagcct atggagaaac tgtatatggt actgatcact      300
accaaaaaca gcaacatttt agaagatttg gagaccctaa ggctcttctc aagagtgtac      360
cctgaatatt gcgagcctta gaagagaatg aaatatctga gcactgnttt gatttgattt      420
ttgcttttga tgaaaaatgc gcactgggat acccgggang aatgttaact tggcacagat      480
canaaccttt cacagaaaaa

```

```

<210> 356
<211> 511
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

```

```

<400> 356
gggcttctgc tgagggggca ggcggagctt gaggaaaccg cagataagtt tttttctctt      60
tgaaaagatag agattaatac aactacttaa aaaatatagt caataggtta ctaagatatt      120
gcttagcgtt aagittttta cgtaatTTta atagcttaag attttaagag aaaaatgaa      180
gacttagaag agtagcatga ggaaggaaaa gataaaaagt ttctaaaaa tgacggaggt      240
tgagatgaag cttcttcacg gagtaaaaaa tgtattttaa agaaaatgga gagaaggac      300
tacagagccc cgaatttaata ccaatagaag ggcaatgctt ttgatttaaa atgaagggtga      360
cttaaacacg ttaaaagtta nttaaagaat tgtagggtgat taaaataatt tgaaggcgat      420
cttttaaaaa gagattaaac ccgaagggtga ttaaaagacc ttgaaatcca tgacgccagg      480
gagaattgcc gtcattttaa gcttagttaa c

```

```

<210> 357
<211> 511
<212> DNA
<213> Homo sapien

```

```

<220>

```

<221> misc\_feature  
 <222> (1)...(511)  
 <223> n = A,T,C or G

<400> 357  
 gatacttcac atttccctag ggaacgggagc ccgaggggggc cgttcggccc tcttccctctc 60  
 gctggggcga caccocgctg taggaccgta acccttagtc ccaatgcctc cgttaagcga 120  
 gttgagtggg tgccctgggt tggagctgtg gaggtgtccc cggtagcgag cgcggccaga 180  
 actgcggtca cttaagtttt ccgtgtgcgg gttgcaagga cggtagcggtc gctcgtgata 240  
 atttggcttc ctgagattct gcttacaaga aaggagtggg aaataccctt ggaagaaaaa 300  
 ctaaaaacagt aagaaaacca aaacttattt ttacatggnt gtcagcacat ttaccgatat 360  
 ggacactttt cccaataatt tctcctgtgt ggagacagt gattgacagg ttctcagtcg 420  
 gaattccaga aaaatgttaa ttgatgaaa gggtacnag tgagcatcat aaagntaatt 480  
 attaanacac tgaaggctga acacacaagg g 511

<210> 358  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(401)  
 <223> n = A,T,C or G

<400> 358  
 acggatgaag atgatgacct tcaagaaaat gaagacaata aacaacataa agaaagcttg 60  
 aaaagagtga cctttgtctt accagatgat gcggaaaactg aagatacagg tgttttaaat 120  
 gtataaaaaa attctgatga agttaaatcc tctcttgaaa aaagacagga aaagatgaat 180  
 gaaaaaattg catctttaga aaaagagttg ttagaaaaaa agcccgtggc agcttcaggg 240  
 ggaagtgaac gcacagaaga ggccagagaa caactccttg aggagacctt acctttgcca 300  
 tctgcccagt ggccctgtga ttacagagga acccccttca ctggagattt ctttaacnga 360  
 ngatagagat cngnttggga tatgtntcct taagaaaacc t 401

<210> 359  
 <211> 511  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(511)  
 <223> n = A,T,C or G

<400> 359  
 gcgatgcccg cgcgccagg acgcctcctc ccgctgtgtg ccgcggcggc ggccctgact 60  
 gcgctgctgc tgcgtgtgct gggccatggc ggcgccgggc gctggggcgc cggggccag 120  
 gagggcgcg cgccggcggc ggacggggccc ccgcggcgag acggcgagga cggacaggac 180  
 ccgcacagca agcacctgta caccggcgac atgtttcagc acgggatcca gagcgccgc 240  
 gcaacttcgtc atgtttctcg cgccttggtg tggacacttg ccagcggtct gcagccgagt 300  
 ttggaatgac ctgtggganga acaaatataa cagcatggaa agaattgccaa aagttctatgt 360  
 ggnntaaagt ggacttgcac nggccacttc gactngtgct ccccgaagg gngggagagt 420  
 acccacctta aaacttttca accaaggcaa aaactttgaa aaccagggtct cggattcaaa 480  
 atggaaaaact gatgttcaac ctgaacaaga a 511

<210> 360  
 <211> 511  
 <212> DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(511)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 360

tactgggaga	ctttgagatt	gagtccaaac	agctggaagc	agagtcttgg	agtcggataa	60
tagacagcaa	gtttctaaaa	cagcaaaaaga	aagatgtggt	caaacggcaa	gaagtaatat	120
atgagttgat	gcagacagag	tttcatcatg	tcccgactct	caagatcatg	agtggtgtgt	180
cnagccnggg	gatgatggcg	gatctgnttt	ttgagcanca	gatggtagaa	aaagctggtt	240
ccctgtttgg	atgagcttga	tcagtatccc	ataccatttc	tttccagagg	attcttggag	300
ccggaagaaa	nggagctctc	ttggtgggat	aaaaagttaa	aaagaacttt	ctcttcaana	360
aggatagggg	gatgtgcttt	gtaaaatcan	tttttcaggg	ngganaatgc	cnnaaccggt	420
ttaaagaaaa	acatnttggg	naagtttttg	tgggccaaca	ttaccgggtc	ttgtaaacct	480
accttcaaag	aacctttttg	cccagggtta	a			511

&lt;210&gt; 361

&lt;211&gt; 411

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(411)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 361

gctcagcggc	ccgatcccac	ggaagcggc	tcggaggggg	gggaccgggc	cggaccggag	60
atggcgccgc	cagcgggcgg	ggcgggcgcg	gcggccctcg	acttgggctc	cgccgcagtg	120
ctcttggctg	tgacgcgcgc	ggtgaggccg	ctgggcggcg	ggccagacgc	cgaagcacaa	180
cttgccgagg	ctgcagctta	acgcggaacc	tgagaagcct	ggcgcttncn	gctggaactt	240
cttggcgccg	gacctggggc	ggtaatattg	gtggccctga	gtcattttct	caccattccag	300
gccaccacaa	cgactaagct	cacaagaagg	ctgaactnnc	tgattctnaa	cctagaanta	360
cgtgcatcta	tcagtgcncg	aagaaatgac	aacataccac	tggaactctg	g	411

&lt;210&gt; 362

&lt;211&gt; 511

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(511)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 362

cgggggaccg	ggctgccttg	gcccctcagc	gctcgcgctc	tttccggcag	ttggaacgct	60
tcctgttgtc	ctcacccgta	accgcctggt	gcccctcgtc	tcagagtcoc	tcacgcgtcc	120
ctctccgctt	ttgctcgttt	ggctgcgcgc	gccggggctt	cgccagccct	caagtcgaga	180
ctaactggcc	aaggggcgct	tcgcgctctc	cgccgtcccc	agccctgcct	ctccctgggc	240
ctgcccagtg	caatgacagg	ctcaacacct	tgctcatcca	tgagtaacca	cacaaaggaa	300
agggtgacaa	tgaccaaaag	tgacaactga	gaatttttat	agcaacctta	tcgctcacat	360
gaagaacgag	aaatgagaca	aaagaagtta	gaaaaagggg	atggaagaag	aaggcctaaa	420
aaaatgaagg	agaaaaccaa	cttccgaaga	tcaaccacat	tgcttcggaa	anggaacaaa	480
aanitttctt	cgtttgaan	aaaaacaaan	a			511



<210> 363  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 363  
 caggatctgg ggagaaagag ccccatccct tctctctctg ccaccatttc ggacaccccg 60  
 cagggactcg tttttgggatt cgcactgact tcaaggaagg acgcgaaccc ttctctgacc 120  
 ccagctcggg cgccacactg tctttgcgcg ggtgaccctt ctctcatgac cctgcggtgc 180  
 cttgagccct ccgggaatgg cggggaaggg acgcggagcc agtggggggac cgcggggtcg 240  
 gcggaggagc catcccgcga ggcggcgctt ctggcggaagg ccctgcggga gctcggtcag 300  
 acaggatggt actggggaag tatgactggt aatgaagcca aagagaaatt aaaagaggca 360  
 ccagaaggaa cttttcttgat tagagatagc tcgcattcag a 401

<210> 364  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 364  
 agtcaagggt ttcttttccc tttttaccat ggtttctaca aaaataacct tcaggaaaaa 60  
 gaaaatcagg aaaaaaattt tttttcaata atcttatctc ctatatataa ttagatttga 120  
 agaggattaa cgttgtttta gtttgggtcc agatcagcct tatacaacat ttctaaacct 180  
 attttgactt ttaaaaaaatt taaacacaga ctctctaaat tacttgatgt aagtaattta 240  
 aatcacttat gaccaagtta ttaaccttat gaatcagaag tctgaccctt gtaggaaatt 300  
 atattocact ataaagtaca tcagatcttt gccatatatt gatggttatt atgcataaac 360  
 acattgagtt gtgttggag cagattttata aacctgcatg t 401

<210> 365  
 <211> 361  
 <212> DNA  
 <213> Homo sapien

<400> 365  
 atctggagtt gcacaaatag ttcttttagaa cataaaacta aatggattta tacataacag 60  
 ttacattcag catttaagag aggcagttaca aaaatgtggt ctgcttttat ctgatataaa 120  
 ttgcatgtaa taccatgatt taaacaatat cagttatatt aactaatgcc atgagatata 180  
 tctttcagc aacgtctgctg gtttccata atagacagaa aaaaatgcagt tgtatgagca 240  
 actgagtttc ttttcatctt caaattcatt tgtgatgggt ggaagatcta aggacaatcc 300  
 ttccattgaa gaagtaggaa aaacagttca gcactgttct gaactcatca aaaaatgaaat 360  
 t 361

<210> 366  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 366  
 cgggagcagc agaggctctag cagccggggc cgcggggccg ggggcctgag gaggccacag 60  
 gacggcgctc ttcccggcta gtggagccgc cgcgggggcc cgtgcggccc gcaccgtgag 120  
 gggaggaggc cgaggaggac gcagcgccgcg ctgcggcgcg gaggaagcgc tccaccaggg 180  
 ccccgcagcg cactcgttta accacatccg cgctctctgct ggaacgcgtt gctgcgcgct 240  
 gtccacgggt ccctccattt tgaaggaggaa aaaggctctc cccaccattt cccctgcccc 300  
 taggagctgg agccggagga gccgcgctca tggcggttcag ccogtggcag atcctgtccc 360  
 ccgtgcagtg ggcgaatagg acgtggtctg cggtaacgcg c 401

<210> 367

<211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 367  
 catggagtcg ggcaagatgg cgcctcccaa gaacgctccg agagatgcct tgggtgatggc 60  
 acagatccctg aaggatatgg gaatcacaga gtatgaacca aggggttataa atcaaatgtt 120  
 ggaattttgtc ttccgttatg tgactacaat tctggatgat gcaaaaattt attcgagcca 180  
 tgctaagaaa cctaattgtg atgcagatga tgtgagactg gcaatccagt gtctgtctga 240  
 ccaatctttt acctctcttc ccccaagaga ttttttactg gatatcgcaa ggcagaaaaa 300  
 tcaaacccctt ttgccactga ttaagccata tgcaggacct agactgccac ctgatagata 360  
 ctgcttaaca gctccaaact ataggctgaa gtccttaatt a 401

<210> 368  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 368  
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 ttaaagttaa gacgctgacc ggaaaggaga ttgagatgta cattgaacct acagacaagg 120  
 tggagcggaat caaggagcgt gtggaggaga aagagggaaat cccccacaa cagcagaggc 180  
 tcatctacag tggcaagcag atgaatgatg agaagacagc agctgattac aagattttag 240  
 gtggttccagt ccttcacctg gtgttggtctc tgagaggagg aggtggtctt aggcagtgat 300  
 ggacctccca ttttacctct ttaccctgtc gctcataatg aggcatacata tatcctctca 360  
 ctctctggga caccatagcc ctgccccctc cctcggtatgc c 401

<210> 369  
 <211> 174  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(174)  
 <223> n = A,T,C or G  
 <400> 369  
 gcgagnnngg gcgcaagcgc ggggcccggag cggccttccc ggagtccttt gcgcggcacc 60  
 tggcgacaaa atggctgccc gagggagacg ggcggagcct cagggccggg aggcctcggg 120  
 cccccggggc ggtggcgggt ggcggagccg ttgggctgag tcgggatcgg ggac 174

<210> 370  
 <211> 375  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(375)  
 <223> n = A,T,C or G  
 <400> 370  
 tgcttttcca actttattta gaaaaacaaa tccaggctcc agtgccccct gtaccctccc 60  
 cgaccccagc cataatttaa ataaactana gacagagtgt gagggagggg acagganagg 120  
 ttgggggtcac ggtggaagga ggaaganagc ccactacagc cgccgcagcg cccgcttctt 180  
 gtccgtcttt ttcttgccg ccagcttctt atcgcgctcg ccagcatgct tnttggccat 240  
 gggaccctca gccctcccg ggcctccctg ggcctccagg tcggtggagg aagcttcagt 300

gccactggcc agggcccgac cggcttcggc cctgccgctg ggcccgccgg cgcccccgtag 360  
gatctctgtg agcag 375

<210> 371  
<211> 375  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(375)  
<223> n = A,T,C or G

<400> 371  
taaattctaa aaaatatttt aatacttgaa aacttctaaa acaaaaggta aggtaacatg 60  
ttctttcaaa agtgaatttc acatgcaaac cattaattat atttatttta ctgngagata 120  
aaagcaaaaac ataacattcg gagaaagaga ccagtaactg acctatttat ttatatattat 180  
attaatgnga atcctcatta gaaatgtgat aaogttattg cacaaacaaa accgtgggca 240  
gaaacatccc agcaatgcag gggcgcccat accgggttac aagggatgtc cagcatgtgt 300  
ttccctggaa cactcanagt ctgcactttt cctgcaaatg ggaccatgtc tgattattta 360  
ttatgaaaga acact 375

<210> 372  
<211> 164  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(164)  
<223> n = A,T,C or G

<400> 372  
cgctctgnt cctcaacctc tacctggcgg aggttatatg taaagtcaag tgtgccactg 60  
aacctgcag acacaaaatt ctactgcatt tgggctttat aatggaagc ctgctctttt 120  
tagtggtgaa cttgacttgc gcaatgctag ttcatggaga tgtc 164

<210> 373  
<211> 401  
<212> DNA  
<213> Homo sapien

<400> 373  
gcgctgttcg cetttgcta ctgcagctg tggcggtctg tctgtaccg cgagoggcg 60  
ctgagttacc agagcctctg cctcttctc tgtctcctgt gggcagcgt caggaccacc 120  
ctcttctcgg cgccttctc gctcagcgge tccctgccct tgcctcgccg gcccgctcac 180  
ctgcaactct tcccacaact gctgctctac tgcctccct cctgtctcca gttctccacg 240  
ctctgtctcc tcaacctcta cctggcgagg gttatatgta aagtcagatg tgcactgaa 300  
cttgacagag acaaaattct actgcatttg ggctttataa tggcaagcct gctcttttta 360  
gtggtgaact tgaactgcgc aatgctagtt catggagatg t 401

<210> 374  
<211> 401  
<212> DNA  
<213> Homo sapien

<400> 374  
ggaatgatac cattcagatt gatttgaga ctggcaagat tactgatttc atcaagttcg 60

acactggttaa	cctgtgtatg	gtgactggag	gtgctaacct	aggaagaatt	ggtgtgatca	120
ccaaacagaga	gaggcacccct	ggatcttttg	acgtggttca	cgtgaaagat	gccaatggca	180
acagctttgc	cactcgactt	tccaacattt	ttgttattgg	caaggggcaac	aaaccatgga	240
tttctcttcc	ccgaggaag	ggtatccgcc	tcaccattgc	tgaagagaga	gacaaaagac	300
tgggcgccaa	acagagcagt	gggtgaaatg	ggtccctggg	tgacatgtca	gatctttgta	360
cgtaattaaa	aatattgttg	caggattaat	agcaaaaaaa	a		401

<210> 375  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 375						
gagcggagtc	cgctggctga	cccagcgcct	ggtctccgcc	gggaaccctg	gggcatggag	60
aggtctgagt	acctcgcccg	cgccgcacgc	tgcctcgccg	agccaggccg	aggacgtgag	120
ggtggagggc	tcctttcccg	tgaccatgct	tcggggagac	ggtgtggggc	ctgagctgat	180
gcacgcgcgc	aaggaggtgt	tcaaggctgc	cgctgtccca	gtggagttcc	aggagcacca	240
ccctgagtgc	gtgcagaata	tggcatctga	ggagaagctg	gagcaggctg	tgagttccat	300
gaaggagaa	aaagtggcca	tcatttgaaa	gattcatacc	ccgatggagt	ataaggggga	360
ctagcctcc	tatgatatgc	ggctgaggcg	taagttggac	t		401

<210> 376  
 <211> 284  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(284)  
 <223> n = A,T,C or G

<400> 376						
ggaacaagg	cgtgaaaaa	aaggtcttgg	tgagggtccg	ccatttcac	tgctctcatt	60
ctctgcgcct	ttccagagc	ttccancagc	tggtatgttg	ggccagagca	tcgggaggtt	120
cacaacctct	gtggtccgta	ggagccacta	tgaggagggc	cctgggaaga	atttgccatt	180
ttcagtgtaa	aacaagtgtt	cgttactagc	taagatgtgt	ttgtactttg	gatctgcatt	240
tgctacaccc	ttcctgtan	taagacacca	actgcttaaa	acat		284

<210> 377  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 377						
atattatgta	ttgcactctc	ggtgtgattt	atcgtatgta	tctgataggt	tttatgaatt	60
gttttgagtt	gtaaaactcct	atacccttta	ttaaaatgga	cctaatttaag	tgatttatgc	120
tttgtgcaat	ttcttaaatc	agatctctct	aggattgaag	ggatccatag	gtatctttca	180
cttagtgtag	agccctagtag	tatactttta	tattcctgaa	gagagaccag	cattaaacata	240
aagagagaa	tcttaggaaa	aaatatacct	aagaattatt	tttaaaatc	atactgtgaa	300
ggagaattctg	cctgcctatt	tcctctccaa	atttcagaaa	ataacacaga	gtgctatttg	360
cctgaacttt	aatgagcttg	actttgttat	gattcaggga	g		401

<210> 378  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 378

ccagaacaca	ggtgtcgtga	aaactacccc	taaaagccaa	aatgggaaag	gaaaagactc	60
atatcaacat	tgtcgtcatt	ggacacgtag	attcggggcaa	gtccaccact	actggccatc	120
tgatctataa	atgcggtggc	atcgacaaaa	gaaccattga	aaaatttgag	aaggaggctg	180
ctgagatggg	aaagggctcc	ttcaagtatg	cctgggtctt	ggataaacctg	aaagctgagc	240
tgtaacgtgg	tatcacattt	gatatctcct	tgtggaaatt	tgagaccagc	aagtactatg	300
tgactatcat	tgtatgcccc	ggacacagag	actttatcaa	aaacatgatt	acaggggacat	360
ctcaggctga	ctgtgctgtc	ctgattgttg	ctgctgggtg	t		401

&lt;210&gt; 379

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 379

tcagatatca	ggtggcttct	tcaaatgatt	tttaagtatc	tcgatgatga	tgaagaacaa	60
agacatcaat	caggattcag	gaagacagct	tttgcggaag	atgcttaag	ggaagcatca	120
aggattgggt	ttgatatttg	aaagtttaag	agtgggtatac	ttttattcag	tcaacacatg	180
acaaatgtaa	aaggcactca	tttgtgttgc	ctggaagaag	cctgggcagca	ttccattcag	240
acatctgccc	tttcatcgct	ccacttttta	cttattgcag	tcctttcagt	ctgaatatatt	300
cctcctgaag	catcttctgc	ogtcggaat	gactccctgc	tccagatcc	tgtagccctt	360
attattgaca	cctttcattt	agaaatttag	cacatgtcac	a		401

&lt;210&gt; 380

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 380

cctgactctc	tgaggctcat	tttgcagttg	ttgaaattgt	ccccgcagtt	ttcaatcatg	60
tctgaaccaa	tcagagtcc	tgtgactgga	gcagctggtc	aaattgcata	ttcactgtctg	120
tacagtattg	gaatggatc	tgtctttggt	aaagatcagc	ctataattct	tgtctgtgtg	180
gatatacccc	ccatgatggg	tgtcctggac	ggtgtcctaa	tggaaactgca	agactgtgcc	240
cttccctccc	tgaagaatgt	catcgcaaca	gataaagaag	acgttgccct	caaagacctg	300
gatgtggcca	ttcttgtggg	ctccatgcca	agaaggggaag	gcattggagag	aaaagattta	360
ctgaagaagca	atgtgaaaat	cttcaaatcc	cagggtgcag	c		401

&lt;210&gt; 381

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(401)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 381

ggggcttcgc	tggcagtcgt	aacggcaagc	ttgagcaacg	cggtaaaaat	attgcttcgg	60
tgggtgacgc	ggtacagctg	tccaagggcn	ttngtaacgg	gaatgccgaa	gcgtgggaaa	120
aaggagagcg	tggcggaaga	cggggatgag	ctcaggacag	agccagaggc	caagaagagt	180
aagacggccg	caagaaaaaa	tgacaaagag	gcagcaggag	agggcccagc	cctgtatgag	240
gacccccag	atcagaaaaa	ctcaccagct	ggcaaacctg	ccacactcaa	gatctgctct	300
tggaaatgtg	atgggcttcg	agcctggatt	aagaagaag	gatttagattg	ggtaaaaggaa	360
gaagccccag	atatactgtg	ccttcaagag	acccaatgtt	c		401

&lt;210&gt; 382

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 382

gagcagcccc	cggcggtgta	aagccggggc	agaagtgtct	gtctcggtcg	ggattccggg	60
cttggtccca	cagagcggtg	gactgcggtg	ggagggaaga	ggttttgagc	gcgctggcct	120
ccgcgcgtcg	tgcattgcag	cattatttca	gttcaaaatg	aactatatgc	ctggcacccg	180
cagcctcatc	gaggacattg	acaaaaagca	cttggttctg	cttcgagatg	gaaggacact	240
tataggcttt	ttaagaagca	ttgatcaatt	tgcaaaacta	gtgctacatc	agactgtgga	300
gcgtattcat	gtgggcaaaa	aatacgttga	tattcctcga	gggatttttg	tggtcagagg	360
agaaaatgtg	gtcctactag	gagaaaatga	cttggaaaag	gagagtgcga	caccctccca	420
gcaagtatcc	attgaagaaa	ttctagaaga	acaaagggtg	gaacagcaga	ccaagctgga	480
agcagagaag	t					491

&lt;210&gt; 383

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 383

gagtccatct	cagcgctgtg	aaaaatgcagt	gaaaaaacct	gaagataaaa	aggaagtgtt	60
cagacccctc	aagcctcgtg	gcgaagtggg	tctgaccgca	ctggccaaag	agcttcgagc	120
agtgggaagt	gtacggccac	ctcacaaagt	aacggactac	tcctcatcca	gtgaggagtc	180
ggggacgagc	gatgaggagg	acgacgatgt	ggagcaggaa	ggggctgacg	agtcacacct	240
aggacccagc	gacaccagag	acgcgtcatc	tctgaatttg	agcaatgggt	aaacggaatc	300
tgtgaaaacc	atgattgtcc	atgatgatgt	agaaaagtga	cgggccatga	ccccatccaa	360
ggaggggcact	ctaactcgtc	gccagagtac	agttgaccaa	aagcgtgcca	gccatcatga	420
gagcataggc	tttgccggtc	gcattcacct	cttgccagat	ctcttacagc	aaagccattc	480
ctcctccaat	t					491

&lt;210&gt; 384

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 384

gagcctaact	tcaggtgtgtc	caccgcgagc	coccttgagca	ccaaccctag	tcccccgccg	60
gcgtccctat	tcgctccgag	aaggtacaaa	aaggctctgg	acggcgcggt	ggttaggagga	120
cgggagcggg	ggcggggaagt	tccttgaaag	agcgagacag	ggaggggacag	ggcagaggag	180
gagaggaagg	cgatgcgacg	gacaggcgca	cccgctcagg	ctgactctcg	ggggcgagggt	240
cgagccaggg	gcggctgcgc	tgggggcgag	gcgagcgtgt	ctcaacctcc	acctcgccgc	300
ggaaccggag	gacaggagcc	tcagatgaaa	gaaacaatca	tgaaccagga	aaaactcgcc	360
aaactcgagg	cacaagtgcg	cattgtgtgg	aaagggaact	ctgcgagaaa	gaaggaaggtg	420
gttcatagaa	cagccacagc	agatgacaaa	aaacttcagt	tctccttaaa	gaagttagggt	480
gtaacaata	t					491

&lt;210&gt; 385

&lt;211&gt; 483

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 385

agcccgctgc	aagggtgacg	cgcgcattgtc	tgcgcattctg	caatggatgg	tcgtgcggaa	60
ctgctccagt	ttcctgatca	agaggaaata	gcgacacctac	agcactgagc	ccaataaact	120
gaaggcccgcc	aattctcttc	gctacacacg	actgattccac	cgcaagactg	tgggcggtgga	180
gcggcgagcc	gacggcaaa	gtgtcgtgg	ggtcattaa	cggagatccg	gccacgggaa	240
gcctgccacc	tcctatgtgc	ggaccacccat	caacaagaat	gctcgcgcca	cgctcagcag	300
catcagacac	atgatccgca	agaacaagta	cgcgcccgac	ctgcgcatgg	cagccatccg	360
cagggccagc	gccatcctgc	gcagccagaa	gcctgtgatg	gtgaagagga	agcggaccgc	420

```

ccccaccaag agctcctgag cccctctgcc ccagagcaat aaagtcagct ggctttctca 480
cct 483

```

```

<210> 386
<211> 491
<212> DNA
<213> Homo sapien

```

```

<400> 386
agggtggaag aaaaaacata aatgaagtta atgcacttct tttcctagcc caaaagtcac 60
tgtgattata tttttttaat gaagtttaga aaaaagctg ttgtctctc aattgtaaaa 120
ttagtttcaa aatgctgctt ctcttatcat tagtctagta attgttgaa tttctgtcaa 180
actgcatttt acaaaattga aacttggaag ctgtattaac ttttatagtt aaacattgta 240
ttaataaac tatactataa taaacagttt ggttttgat tttttaatt gtattatcca 300
gcctttttaa aattaaaagc taataatga aaataaacca attaaaacat acttttaact 360
tcagatatac aggtatttac attatgaaaa aactgaacaa agttttaaca atactgagct 420
ttaagaattt agccagcagg gaaaatttcc aggtttgaga atgttctaata gtaaatattt 480
aatcataata c 491

```

```

<210> 387
<211> 491
<212> DNA
<213> Homo sapien

```

```

<400> 387
ccacaccacc gtgtcccaag tccagccccc tccctccaag gcatcagcac ctgaaccccc 60
tgcaagaaga gaagtggcaa ctggtacaac ctacgctctc gatgaccttg aagccctggg 120
tacaactgagc ctggggacca cagaggagaa ggcagcagct gaggcggctg tgcccaggac 180
cattggggccc gagctgatgg agctgggtgcg gagaacacat ggcctgagcc acgaattatg 240
ccgggtggccc atcggcatca tagtgggtca catccaggcc tcggtgccgg ccagctcaacc 300
agtcagtggc caggtctctcc tctcactcgt agagggcagg gacctcagca tggccctgcc 360
ctcagggcag gtctgccacg accagcagag gctggagggt atctttgcag acctggctcg 420
ccggaaggac gacgcccagc agcgcagttg ggcactatat gaggatgagg gtgtcatccg 480
ctgctaceta g 491

```

```

<210> 388
<211> 491
<212> DNA
<213> Homo sapien

```

```

<400> 388
gagactatca aactcctgag ccaacaactt aatatgacta gcttacacaa tagcttttat 60
agtaagata cctctttacg gactccactt atgactccct aaagcccatg tcgaagcccc 120
catcgctggg tcaatagtag ttgccgcagt actcttgaaa ctaggcggtc atgggataat 180
acgcctcaca ctcatctcca accccctgac aaaacacata gcctacccct tcctttgta 240
atccctatga ggcataatta taacaagctc catctcgcta cgacaaacag acctaaaatc 300
gctcattgca tactcttcaa tcagccacat agccctcgta gtaacagcca ttctcatcca 360
aaccctctga agcttcaccc gcgcagtcac tctcataatc gccacgggac ttacatctct 420
attactattc tgcttagcaa actcaacta cgaacgcact cacagtcgca tcataatcct 480
ctctcaagga c 491

```

```

<210> 389
<211> 511
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

&lt;222&gt; (1)...(511)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 389

tactgata	tctttaa	tattcat	caagttt	ggt	canaac	caagag	60
gaaagaaa	ataattc	ttttaa	ctgtctg	cc	aaagtata	atatgaa	120
atgcattat	ctnttag	acaaa	tcaaa	ttt	gggtatta	aagttca	180
ttcanacta	cctcaa	agga	ctgtt	taag	tgcaana	agtttcat	240
caattatt	ttt	acana	atgc	tgga	gtgca	attt	300
ggnntctg	aa	aatgaaa	ctg	tgaa	atgtt	tggtgtt	360
atctctgt	tgtatc	ga	aatat	tgga	tgtat	ctgtg	420
gcaatgg	cct	tcttcag	ggc	tttctc	ccct	gttccag	480
ctccctag	ct	tcaacc	acat	ggagg	cca	ctgtag	511

&lt;210&gt; 390

&lt;211&gt; 1984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 390

cctggggtta	gaggctggg	tggtggggg	gtaaggggg	agtccttctc	cccttcga	60
gcggctccga	gtccagcccc	ttcttcccg	cgctcgtcg	ccggccccc	agccccctca	120
tgagggtg	ctgccgggt	ccggcggcg	ctgccgccc	cgcagccgc	cgcgagccct	180
ccacgccc	cgggggcag	ggaggcgag	gcgcgctgc	tgacgctca	ggcgccggg	240
tgccgggtc	cgctcagttg	gcgctgagc	ctctgcacg	cctgctctac	gcgcgctgt	300
tcgcctttg	ctacctgcag	ctgtggcgc	tgctcctgta	ccgcgagcg	cggtgagtt	360
accagagct	ctgctcctc	ctctgtctcc	tggtggcagc	gctcagga	accctctct	420
ccgcgcctt	ctcgtcagc	ggctccctgc	ccttgcctcg	gcgcgcgc	caactgca	480
tcttccccc	ctgggtgctc	tactgcttc	cctcctgtct	ccagttctcc	acgctctgtc	540
tctcaacct	ctacctggcg	gaggttatat	gtaaagtca	atgtgccact	gaacttgaca	600
gacacaaa	tctactgcat	ttgggcttta	taatggca	cctgctctt	ttagtgtgta	660
aacttgctg	cgcaactgta	gttcatggag	atgtccaga	aaatcagttg	aagtggactg	720
tgtttgttc	agcattaatt	aatgatgcc	tgttattct	ttgtgccatc	tcttttagtgt	780
gttcatatg	caaaattaca	aaaatgtcat	cagctaagt	ctacctcgaa	tcaaaaggta	840
gttctctgt	ccagactgtc	atcgtgggt	ctgtagtc	tcttctgtac	tcttccagag	900
gttgttata	tttgggtgtg	gtcacccat	ctcaggata	atatagaagt	ccattttaatt	960
atggctgga	taattcttca	gataaggctc	atgtagaaga	cataagtgga	gaagagtata	1020
tagtatttg	aatggtcctc	tttctgtgg	aaatgtgccc	agcatgtgctg	gtggtactgt	1080
ttttccgggc	acagagatta	aaccagaatt	tggaacotgc	tggaatgata	aatagtcaca	1140
gttatagttc	cagagcttac	tttttcgaca	atccaagacg	atatgatagt	gatgatgacc	1200
tgccaagact	gggaagttca	agagaaggaa	gtttaccaaa	ttcgcaagt	ttgggctggt	1260
atggcaccat	gactgggtgt	ggcagcagca	gttacacagt	cactccccc	ctgaatggac	1320
ctatgacaga	tactgtcct	ttgtcttcta	ctgttagtaa	tttagatttg	aaacatcatc	1380
atagcttata	tgtagaccca	caaaactgac	agcatcacca	agtcagatt	cttgcaattg	1440
ttttcataaa	tgtgtatatt	caatgtgttt	aaattccatc	tacataaaca	ttccattatt	1500
ttttgcaact	gaaaacaaa	ctggaagtg	tggtgtgtgt	tggtataata	ccacagctatt	1560
atgtttgacc	tcttcatagt	aaaatgga	aaaatggaaa	tttggagta	ggagaaaaga	1620
gagattagat	cttaaggcac	ttgatggcct	ccaaaatcc	tgactttgga	catcacaagt	1680
catatgtcca	cttttatctt	tgttctgagt	cactgcagtc	cccaagtca	atgtccaagt	1740
ttcacactga	aatactgtat	tgtacaccaa	actggaaggg	aattttcccta	tgaanaatcaa	1800
agccgggtata	ttcatgtgta	tgctctatac	agatatctta	ataaaaaatt	atatgtgtga	1860
acagtgcaca	gagttaaagg	ataaaaaatgt	atcattcttt	ataaaaaatc	actgaaaagt	1920
tgtatacatt	gaagacagtt	cttttaagca	tgatttttaa	atagcaactg	aaatttcaatc	1980
at						1984

&lt;210&gt; 391

&lt;211&gt; 429

&lt;212&gt; PRT



&lt;213&gt; Homo sapien

&lt;400&gt; 391

```

Met Arg Val Ser Val Pro Gly Pro Ala Ala Ala Ala Pro Ala Ala
      5      10      15
Gly Arg Glu Pro Ser Thr Pro Gly Gly Gly Ser Gly Gly Gly Gly Ala
      20      25      30
Val Ala Ala Ala Ser Gly Ala Ala Val Pro Gly Ser Val Gln Leu Ala
      35      40      45
Leu Ser Val Leu His Ala Leu Leu Tyr Ala Ala Leu Phe Ala Phe Ala
      50      55      60
Tyr Leu Gln Leu Trp Arg Leu Leu Tyr Arg Glu Arg Arg Leu Ser
      65      70      75      80
Tyr Gln Ser Leu Cys Leu Phe Leu Cys Leu Leu Trp Ala Ala Leu Arg
      85      90      95
Thr Thr Leu Phe Ser Ala Ala Phe Ser Leu Ser Gly Ser Leu Pro Leu
      100      105      110
Leu Arg Pro Pro Ala His Leu His Phe Phe Pro His Trp Leu Leu Tyr
      115      120      125
Cys Phe Pro Ser Cys Leu Gln Phe Ser Thr Leu Cys Leu Leu Asn Leu
      130      135      140
Tyr Leu Ala Glu Val Ile Cys Lys Val Arg Cys Ala Thr Glu Leu Asp
      145      150      155      160
Arg His Lys Ile Leu Leu His Leu Gly Phe Ile Met Ala Ser Leu Leu
      165      170      175
Phe Leu Val Val Asn Leu Thr Cys Ala Met Leu Val His Gly Asp Val
      180      185      190
Pro Glu Asn Gln Leu Lys Trp Thr Val Phe Val Arg Ala Leu Ile Asn
      195      200      205
Asp Ser Leu Phe Ile Leu Cys Ala Ile Ser Leu Val Cys Tyr Ile Cys
      210      215      220
Lys Ile Thr Lys Met Ser Ser Ala Asn Val Tyr Leu Glu Ser Lys Gly
      225      230      235      240
Met Ser Leu Cys Gln Thr Val Ile Val Gly Ser Val Val Ile Leu Leu
      245      250      255
Tyr Ser Ser Arg Ala Cys Tyr Asn Leu Val Val Val Thr Ile Ser Gln
      260      265      270
Asp Thr Leu Glu Ser Pro Phe Asn Tyr Gly Trp Asp Asn Leu Ser Asp
      275      280      285
Lys Ala His Val Glu Asp Ile Ser Gly Glu Glu Tyr Ile Val Phe Gly
      290      295      300
Met Val Leu Phe Leu Trp Glu His Val Pro Ala Trp Ser Val Val Leu
      305      310      315      320
Phe Phe Arg Ala Gln Arg Leu Asn Gln Asn Leu Ala Pro Ala Gly Met
      325      330      335
Ile Asn Ser His Ser Tyr Ser Ser Arg Ala Tyr Phe Phe Asp Asn Pro
      340      345      350
Arg Arg Tyr Asp Ser Asp Asp Asp Leu Pro Arg Leu Gly Ser Ser Arg
      355      360      365
Glu Gly Ser Leu Pro Asn Ser Gln Ser Leu Gly Trp Tyr Gly Thr Met
      370      375      380
Thr Gly Cys Gly Ser Ser Ser Tyr Thr Val Thr Pro His Leu Asn Gly
      385      390      395      400
Pro Met Thr Asp Thr Ala Pro Leu Leu Phe Thr Cys Ser Asn Leu Asp
      405      410      415
Leu Asn Asn His His Ser Leu Tyr Val Thr Pro Gln Asn
      420      425

```

```
<210> 392
<211> 1584
<212> DNA
<213> Homo sapiens
```

[illegible]

```
<210> 393
<211> 191
<212> PRT
<213> Homo sapiens
```

Met	Gly	Lys	Ser	Cys	Lys	Val	Val	Val	Cys	Gly	Gln	Ala	Ser	Val	Gly
				5					10					15	
Lys	Thr	Ser	Ile	Leu	Glu	Gln	Leu	Leu	Tyr	Gly	Asn	His	Val	Val	Gly
			20					25					30		
Ser	Glu	Met	Ile	Glu	Thr	Gln	Glu	Asp	Ile	Tyr	Val	Gly	Ser	Ile	Glu
		35					40					45			
Thr	Asp	Arg	Gly	Val	Arg	Glu	Gln	Val	Arg	Phe	Tyr	Asp	Thr	Arg	Gly
	50					55					60				
Leu	Arg	Asp	Gly	Ala	Glu	Leu	Pro	Arg	His	Cys	Phe	Ser	Cys	Thr	Asp
	65				70					75				80	
Gly	Tyr	Val	Leu	Val	Tyr	Ser	Thr	Asp	Ser	Arg	Glu	Ser	Phe	Gln	Arg
			85					90						95	
Val	Glu	Leu	Leu	Lys	Lys	Glu	Ile	Asp	Lys	Ser	Lys	Asp	Lys	Lys	Glu
		100						105					110		
Val	Thr	Ile	Val	Val	Leu	Gly	Asn	Lys	Cys	Asp	Leu	Gln	Glu	Gln	Arg
		115					120					125			
Arg	Val	Asp	Pro	Asp	Val	Ala	Gln	His	Trp	Ala	Lys	Ser	Glu	Lys	Val
	130					135					140				

Lys Leu Trp Glu Val Ser Val Ala Asp Arg Arg Ser Leu Leu Glu Pro  
 145 150 155 160  
 Phe Val Tyr Leu Ala Ser Lys Met Thr Gln Pro Gln Ser Lys Ser Ala  
 165 170 175  
 Phe Pro Leu Ser Arg Lys Asn Lys Gly Ser Gly Ser Leu Asp Gly  
 180 185 190

<210> 394  
 <211> 1937  
 <212> DNA  
 <213> Homo sapiens

<400> 394  
 ccggttcccc cagctctggg taccgggctc tgcacgcgt cgccatgatg ggccatcgct 60  
 cagtgctcgt gctcagccag aacacaaagc gtgaatccgg aagaaaagtt caatctggaa 120  
 acatcaatgc tgccaagact attgcagata tcatccgaac atgtttggga cccaagtcca 180  
 tgatgaagat gcttttggac ccaatgggag gcatttgtgat gaccaatgat ggcaatgcca 240  
 ttcttcgaga gattcaagtc cagcatccag cggccaaagtc catgatcgaa attagccgga 300  
 ccaggatga agaggttggg gatggggacca catcagtaat tattcttgca ggggaaatgc 360  
 tgtctgagc tgagcacttc ctggagcagc agatgcaccc aacagtgggt atcagtgctt 420  
 accgcgaagg attggatgat atgatcagca ccctaaagaa aataagtatc ccagtcgaca 480  
 tcagtgcacg tgatatgatg ctgaacatca tcaacagctc tattactacc aaagccatca 540  
 gtccgttggtc atctttggct tgcaacattg ccttggatgc tgtcaagatg gtacagtttg 600  
 aggagaatgg tcggaaaagag attgacataa aaaaatatgc aagagtggaa aagataacctg 660  
 gaggcacatc tgaagactcc tgtgtcttgc gtggagtcac gattaacaag gatgtgacct 720  
 atccacgtat gcggcgctat atcaagaacc ctgcgattgt gctgcgtgat tcttctctgg 780  
 aatacaagaa aggagaagac cagactgaca ttgagattac acgagaggag gacttccacc 840  
 gaattctcca gatgagagaa gagtacatcc agcagctctg tgaggacatt atccaactga 900  
 agcccgatgt ggtcatcact gaaaagggca tctcagatgt agctcagcac taccttatgc 960  
 ggcccaaatc cacagccatc ccagagatcc ggaagacaga caataatcgc attgctagag 1020  
 ccgtgtgggg ccggatagtc agccgaccag aggaactgag agaagatgat gtggaacacg 1080  
 gagcaggccct gttggaatc aagaaaattg gagatgaata ctttacttcc atcactgact 1140  
 gcaaaagacc caaggcctgc accattctcc tccggggggc tagcaaaagag attctctcgg 1200  
 aagtagaagc caacctccag gatgccatgc aagtgtgtcg caatgttctc ctggaccctc 1260  
 agctggtgcc agggggtggg gcctccgaga tggctgtggc ccactgcctg acagaaaaat 1320  
 ccaaggccat gactgtgttg gaacaatggc catcacgggc tgttgcccg gccctagagg 1380  
 tctactctcg taccctgatc cagaactgtg ggccagcac catcctccg tctacctccc 1440  
 ttccggccaa gcacaccag gagaactgtg agacctggg tgtaaatggt gagacgggta 1500  
 ctttgggtga catgaaggaa ctgggcatat gggagccatt ggctgtgaag ctgcagactt 1560  
 atagacagc agtgagagcg gcagtctcgc tactgcgaat tgatgacatc gtttcaggcc 1620  
 acaaaaagaa aggcgatgac cagagccggc aaggcggggc tctgtgatgt ggccaggagt 1680  
 gagtgtctag caagctgact tcaatgcaca gaaccagcag agctccccc ttctctgagc 1740  
 cagagtgcga ggaacactgt ggaactcttt gttcagaagg ctacaggttg gggggcagcc 1800  
 ccagtcacct ttctgtccca gctcagtttt ccaaaagaca catcactgta attctctct 1860  
 attgtaaggt ttccatttag ttgtctccg atgattaaat ctaagtcaat tgaaaaaaa 1920  
 aaaaaaaaaa actcagag 1937

<210> 395  
 <211> 1675  
 <212> DNA  
 <213> Homo sapiens

<400> 395  
 gcgcgaatcg cggctcgcgag ccatggagga ggaggcatcg tccccggggc tgggctgcag 60  
 caagccgcac ctggagaagc tgaccctggg catcacgcgc atccatagaat ctccccagg 120  
 tgtgactgag gtgacatca tagaaaaagc tctgtctgaa cgtcatatga tttcttctg 180  
 ggaacaaaag aataactgtg tgatgcctga agatgtgaag agtctcttacc tttgatccaa 240  
 tggcttccac atgacatgga gtgtgaagct ggatgagcac atcattccac tgggaagcat 300

```

ggcaattaac  agcatctcaa  aactgactca  gctcaccag  tcttccatgt  attcacttcc  360
taatgcacc  acctctggcag  acctggagg  cgatacacat  gaagccagtg  atgatcagcc  420
agagaagcct  cacttttgact  ctgcagtg  gatatttgag  ctggatcatc  gcaatggcag  480
tgggaaagtt  tgcccttgct  acaaaagtgg  gaaaccagca  ttacgagaag  acactgagat  540
ctgggtctctg  gacagagcgt  tatactggca  tttttcaca  gacaccttta  ctgcctatta  600
ccgcctgctc  atcacccacc  tgggcctgcc  ccagtgccaa  tatgccttca  ccagctatgg  660
cattagccca  caggccaagc  aatggttcag  catgtataaa  cctatcacct  acaacacaaa  720
ctgcctcaca  gaagagaccg  actcctttgt  gaataagcta  gccccagca  aagtggttaa  780
gagcaagaac  aagatcgtaa  tcccaaaaa  gaaagggcct  gtgcagcctg  caggtggcca  840
gaaagggccc  tcaggaccct  ccggtccctc  cacttccctc  acttctaaat  cctcctctgg  900
ctctggaacc  cccacccgga  agtgagcacc  cctccctcca  actccctacc  agctccagag  960
tggttggttc  catgcacaga  tggccctagg  ggtgacctcc  agttttgcgt  gtggaccgta  1020
ggcctcttct  tagttgaatg  accaaaattg  taaggctttt  agtcccaccg  acattagcca  1080
ggctcgtagt  gaggcctcca  gagcaggttg  tgctgtcccc  tgccctcgga  agcaatgggg  1140
aatttggaat  ctgtgtgaag  tgcccataa  agtctgagtg  ctttcctctt  ctccaacct  1200
caaccctcaa  tcccttagca  ctgattgatt  agagaggttc  cccaagaaa  ccactggttt  1260
tgaccctaga  agcattagaa  ctgcattggt  cattcaggag  ccactagtca  catatgacta  1320
tttaaattta  aagtaaatgt  tatgaaaaat  tcatttcttc  aattgcatta  gccacatttt  1380
gagtattcat  gtggcttgta  gattctgtat  tagcacaaag  atatggaaca  ttccatcac  1440
cacagaagt  tctgttgac  agcactgc  tagaataatt  tcatactgct  ctctctcaat  1500
taatttttgt  tgttaattgt  gatgtcttca  ttggaatggg  cataatgttc  catgaaacct  1560
ctcaagtaca  caattgtatg  ttctttgtat  cccctaccac  aatatctcgt  ctctgtcat  1620
ttcttttgca  gcttctata  aagtttgtct  tctctatcaa  aaaaaaaaa  aaaaa  1675

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&lt;210&gt; 396

&lt;211&gt; 559

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 396

```

Gly Ser Pro Ser Ser Gly Tyr Pro Ala Leu His Arg Val Ala Met Met
                    5              10              15
Gly His Arg Pro Val Leu Val Leu Ser Gln Asn Thr Lys Arg Glu Ser
                    20              25              30
Gly Arg Lys Val Gln Ser Gly Asn Ile Asn Ala Ala Lys Thr Ile Ala
                    35              40              45
Asp Ile Ile Arg Thr Cys Leu Gly Pro Lys Ser Met Met Lys Met Leu
                    50              55              60
Leu Asp Pro Met Gly Gly Ile Val Met Thr Asn Asp Gly Asn Ala Ile
                    65              70              75
Leu Arg Glu Ile Gln Val Gln His Pro Ala Ala Lys Ser Met Ile Glu
                    80              85              90
Ile Ser Arg Thr Gln Asp Glu Glu Val Gly Asp Gly Thr Thr Ser Val
                    95              100              105
Ile Ile Leu Ala Gly Glu Met Leu Ser Val Ala Glu His Phe Leu Glu
                    110              115              120
Gln Gln Met His Pro Thr Val Val Ile Ser Ala Tyr Arg Lys Ala Leu
                    125              130              135
Asp Asp Met Ile Ser Thr Thr Lys Lys Ile Ser Ile Pro Val Asp Ile
                    140              145              150
Ser Asp Ser Asp Met Met Leu Asn Ile Ile Asn Ser Ser Ile Thr Thr
                    155              160              165
Lys Ala Ile Ser Arg Trp Ser Ser Leu Ala Cys Asn Ile Ala Leu Asp
                    170              175              180
Ala Val Lys Met Val Gln Phe Glu Glu Asn Gly Arg Lys Glu Ile Asp
                    185              190              195
Ile Lys Lys Tyr Ala Arg Val Glu Glu Lys Ile Pro Gly Gly Ile Ile Glu
                    200              205              210
                    215              220

```

Asp Ser Cys Val Leu Arg Gly Val Met Ile Asn Lys Asp Val Thr His  
 225 230 235 240  
 Pro Arg Met Arg Arg Tyr Ile Lys Asn Pro Arg Ile Val Leu Leu Asp  
 245 250 255  
 Ser Ser Leu Glu Tyr Lys Lys Gly Glu Ser Gln Thr Asp Ile Glu Ile  
 260 265 270  
 Thr Arg Glu Glu Asp Phe Thr Arg Ile Leu Gln Met Glu Glu Glu Tyr  
 275 280 285  
 Ile Gln Gln Leu Cys Glu Asp Ile Ile Gln Leu Lys Pro Asp Val Val  
 290 295 300  
 Ile Thr Glu Lys Gly Ile Ser Asp Leu Ala Gln His Tyr Leu Met Arg  
 305 310 315 320  
 Ala Asn Ile Thr Ala Ile Arg Arg Val Arg Lys Thr Asp Asn Asn Arg  
 325 330 335  
 Ile Ala Arg Ala Cys Gly Ala Arg Ile Val Ser Arg Pro Glu Glu Leu  
 340 345 350  
 Arg Glu Asp Asp Val Gly Thr Gly Ala Gly Leu Leu Glu Ile Lys Lys  
 355 360 365  
 Ile Gly Asp Glu Tyr Phe Thr Phe Ile Thr Asp Cys Lys Asp Pro Lys  
 370 375 380  
 Ala Cys Thr Ile Leu Leu Arg Gly Ala Ser Lys Glu Ile Leu Ser Glu  
 385 390 395 400  
 Val Glu Arg Asn Leu Gln Asp Ala Met Gln Val Cys Arg Asn Val Leu  
 405 410 415  
 Leu Asp Pro Gln Leu Val Pro Gly Gly Gly Ala Ser Glu Met Ala Val  
 420 425 430  
 Ala His Ala Leu Thr Glu Lys Ser Lys Ala Met Thr Gly Val Glu Gln  
 435 440 445  
 Trp Pro Tyr Arg Ala Val Ala Gln Ala Leu Glu Val Ile Pro Arg Thr  
 450 455 460  
 Leu Ile Gln Asn Cys Gly Ala Ser Thr Ile Arg Leu Leu Thr Ser Leu  
 465 470 475 480  
 Arg Ala Lys His Thr Gln Glu Asn Cys Glu Thr Trp Gly Val Asn Gly  
 485 490 495  
 Glu Thr Gly Thr Leu Val Asp Met Lys Glu Leu Gly Ile Trp Glu Pro  
 500 505 510  
 Leu Ala Val Lys Leu Gln Thr Tyr Lys Thr Ala Val Glu Thr Ala Val  
 515 520 525  
 Leu Leu Leu Arg Ile Asp Asp Ile Val Ser Gly His Lys Lys Lys Gly  
 530 535 540  
 Asp Asp Gln Ser Arg Gln Gly Gly Ala Pro Asp Ala Gly Gln Glu  
 545 550 555

&lt;210&gt; 397

&lt;211&gt; 307

&lt;212&gt; PRT

&lt;213&gt; Homo. sapiens

&lt;400&gt; 397

Arg Glu Ser Arg Ser Arg Ala Met Glu Glu Glu Ala Ser Ser Pro Gly  
 5 10 15  
 Leu Gly Cys Ser Lys Pro His Leu Glu Lys Leu Thr Leu Gly Ile Thr  
 20 25 30  
 Arg Ile Leu Glu Ser Ser Pro Gly Val Thr Glu Val Thr Ile Ile Glu  
 35 40 45  
 Lys Pro Pro Ala Glu Arg His Met Ile Ser Ser Trp Glu Gln Lys Asn  
 50 55 60

```

Asn Cys Val Met Pro Glu Asp Val Lys Asn Phe Tyr Leu Met Thr Asn
65          70          75          80
Gly Phe His Met Thr Trp Ser Val Lys Leu Asp Glu His Ile Ile Pro
85          90          95
Leu Gly Ser Met Ala Ile Asn Ser Ile Ser Lys Leu Thr Gln Leu Thr
100         105         110
Gln Ser Ser Met Tyr Ser Leu Pro Asn Ala Pro Thr Leu Ala Asp Leu
115         120         125
Glu Asp Asp Thr His Glu Ala Ser Asp Asp Gln Pro Glu Lys Pro His
130         135         140
Phe Asp Ser Arg Ser Val Ile Phe Glu Leu Asp Ser Cys Asn Gly Ser
145         150         155         160
Gly Lys Val Cys Leu Val Tyr Lys Ser Gly Lys Pro Ala Leu Ala Glu
165         170         175
Asp Thr Glu Ile Trp Phe Leu Asp Arg Ala Leu Tyr Trp His Phe Leu
180         185         190
Thr Asp Thr Phe Thr Ala Tyr Tyr Arg Leu Leu Ile Thr His Leu Gly
195         200         205
Leu Pro Gln Trp Gln Tyr Ala Phe Thr Ser Tyr Gly Ile Ser Pro Gln
210         215         220
Ala Lys Gln Trp Phe Ser Met Tyr Lys Pro Ile Thr Tyr Asn Thr Asn
225         230         235         240
Leu Leu Thr Glu Glu Thr Asp Ser Phe Val Asn Lys Leu Asp Pro Ser
245         250         255
Lys Val Phe Lys Ser Lys Asn Lys Ile Val Ile Pro Lys Lys Lys Gly
260         265         270
Pro Val Gln Pro Ala Gly Gly Gln Lys Gly Pro Ser Gly Pro Ser Gly
275         280         285
Pro Ser Thr Ser Ser Thr Ser Lys Ser Ser Ser Gly Ser Gly Asn Pro
290         295         300
Thr Arg Lys
305

```

&lt;210&gt; 398

&lt;211&gt; 416

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 398

```

agaattcggc acgaggattg cctatctcca gtgcaacaac catcaagtgt gctgaaagtc 60
ttcagccggt tgctgcagca gtggaagaaa ggcctacagg tccagtcttg ataagcaccc 120
ccgactttga ggggcctatg cccagtcgcg cccagagaagc tgaaagtctc cttgcctcaa 180
ccagcaaggga ggagaaggat gaagtgtctc tcatttcac tagcatagca gaagaatgtg 240
aggcttctgt ttccggtgta gttgttgaaa gtgaaaatga gcgagctggc acagtcattg 300
aagaaaaaga cgggagtggc atcatctcta cgagctcggt ggaagactgt gagggccccag 360
tgtccagtgc tgtccctcaa gaggaaggcg acccctcagt cacaccagcg gaagag 416

```

&lt;210&gt; 399

&lt;211&gt; 259

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(259)

&lt;223&gt; n = A,T,C or G

```

<400> 399
caaagaattc ggcacgaggg ggcgacctgc attcggaagt caccgaggcc atgctgtacg 60
aaaagttcag ccccgcgggg cctgtgctgt ncatccgggt ctgccngat atgatcacc 120
gccgtccctt gggctatgcc tacgnaact tccancaacc ggcgcagcgt gatcgggctt 180
tggaaccat gaactttgat gtgattnagg gaaanccaat ccttatcntg tnnnaatcat 240
aggatcctt ctttgacaa 259

```

```

<210> 400
<211> 410
<212> DNA
<213> Homo sapiens

```

```

<400> 400
ggcacgaggg gagagcggac ccagagagc cctgagcagc ccacccgccc cgcgcggcct 60
agttaccatc acaccccggg aggagccgca gctgcgcgag ccggcccccg tcaccatcac 120
cgcaaccatg agcagcgagg ccgagaccca gcagccgccc cgcgcgcgcc cccgcgcgcc 180
ccgcctcctc cgcgcgcgag accaagcccg gcactacggg cagcggcgca gggagcggtg 240
gccccggggc cctcacatcg gcggcgccgt ccggcgggga caagaaggtc atcgcaacga 300
aggttttggg aacagtaaaa tggttcaatg taagggaacg atatggtttc atcaacagga 360
atgacacca ggaagatgta ttgtacacc agactgccat aaagaagaat 410

```

```

<210> 401
<211> 433
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(433)
<223> n = A,T,C or G

```

```

<400> 401
ggnacgagga atcatggcgg ctgcgctgtt cgtgctgctg ggattcgcgc tgcggggcac 60
ccacggagcc tcgggggctg ccggcacagt ctctactacc gtagaagacc ttggctccaa 120
gatactcctc acctgctcct tgaatgacag cgcacacagag gtcacagggc accgctggct 180
gaaggggggg gtgtgtgctga aggagggcgc gctgcccggc cagaaaaacg agttcaaggt 240
ggactccgac gaccagtggg gagagtactc ctgcgtcttc ctcccgcgag ccatgggcac 300
ggccaacatc cagctccacg ggccctccag agtgaagccc gtgaagtctg cagaacacat 360
caacgagggg gagacggcca tgctggctcg caagtacagag tccgtgccac ctgtcactga 420
ctgggcctgg tac 433

```

```

<210> 402
<211> 434
<212> DNA
<213> Homo sapiens

```

```

<400> 402
ggcacgaggg tcggactgag caggacttcc ctatcccag ttgattgtgc agaatacact 60
gctgtcgtct gtctctctat tcaccatggc ttctctctgat atccaggtga aagaactgga 120
gaagcgtgcc tcaggccagg cttttgagct gattctcagc cctcgggtcaa aaggatctgt 180
tcacaattc cccctttccc ctccaaagaa gaagatctt tccctggagg aaattcagaa 240
gaaattagaa gctgcagaag aaagacgcaa gtcccatgaa gctgaggtct tgaagcagct 300
ggctgagaaa cgagagcacg agaagaaggt gcttcagaag gcaatagaag agaacaacaa 360
cttcagtaaa atggcgagaag agaaactgac ccacaaaatg gaagctataa aagagaacgc 420
agaggcaca atgg 434

```

```

<210> 403
<211> 435

```

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 403

```

ggcagcaggga actgctgttg ccattcaaac cattgaggag catcctgcac cttttgactg 60
gagctctttt aagccaatgg gatttgaagt atcattttctg aagtttcttg aggagtctgc 120
agtgaagcag aagaaaaata ctgacaaaaga ccattccgaat actggaaaaca aaaaaggatc 180
ccattcgaat tcaagaaaaa atattgataa gactgctgtg actagtggaa atcatgtatg 240
tccttgtaaa gaaagcgaaa cgtttgtaca gtttgccaat ccatcacagc ttcagtgcag 300
tgataatgta aaaaattgtt tagacaagaa tcttaaagat tgcactgagc ttgtctttaa 360
gcaacttcag gaaatgaaac ctaccgtcag tctgaaaaaa cttgaagtac attcaaatga 420
tcagatatg tctgt

```

&lt;210&gt; 404

&lt;211&gt; 416

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 404

```

aaagaattcg gcacgaggcg cgcctccgcc agcaccaccg ccgcctcctg ccctgcagcc 60
accgccacgc cctgtgtcgc cgcgcctcgc ggaccggctg tatgattagg ccacaattctt 120
caatgagtta acatatctct caattctgtg gtgttcttgg tcacacattt atggagtctt 180
tgaaagggcag ttgagattac tgcagggcac agcacgacct ctatgcagac aagtgaactg 240
tagaaactga ttactgtccc accaagaagc ccccataaga gtggttatcc tggacacaga 300
agtgttgaaat tgaatccac agagcatttt acaagatgtc tgcactggat ggggttaaac 360
tcagtgcact tcttttctgt tggcctcagt attactggat tgaagaattg ctgctt 416

```

&lt;210&gt; 405

&lt;211&gt; 435

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 405

```

ggcagcaggg ctgccggagg gtctgtttta agggcccgcg cgttgccgcc cctctggccc 60
gccatctgct tatcctgtcc gtgtctgctc ggctcctcgc gcctggcgct ccgcgagcct 120
gcgctctact tcaaggagca gtttctggac ggagacgggt ggaacttccg ctggatcgaa 180
tcacaacaca agtccagatt ttggcaaatc ttctcagatt ccggcaagtt ctacggtgac 240
gaggagaaag ataaaggttt gcagacaagc caggatgcac gcttttatgc tctgtcggcc 300
agtttcagac ctttcagcaa caaaggccag acgctgtgtg tgcagttcac ggtgaaacat 360
ggcagaaaca tcgactgtgg gggcggctat gtgaagctgt ttcctaatag tttggaccag 420
acagacatgc acgga

```

&lt;210&gt; 406

&lt;211&gt; 424

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(424)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 406

```

gcccaaaccc actccacctt actaccagac aaccttagcc aaaccattta cccaataaaa 60
gtataggcga tagaaattga aacctggcgc aatagatata gtaccgcaag ggaaagatga 120
aaaattataa ccaagcataa tatagcaagg actaacccct atacctttgc cataatgaat 180
taactgaaa taactttgca aggagagcca aagctaagac ccccgaaacc agcagagcta 240
cctaagaaca gctaaaaagag cacaccgcgc tatgtagcaa aatagtggga agatttatag 300

```



```

gtagaggcgca caaacctacc gagcctgggtg atagctgggtt gtccaagata gaatcttagt 360
tcaacttttaa atttgccacac agaaccctctt aaatcccctt gnaaatttaa ctgntagctc 420
aaag 424

```

```

<210> 407
<211> 423
<212> DNA
<213> Homo sapiens

```

```

<400> 407
gctcctaccg gcgcacgtgg tgccgccgct gctgcctccc gctcgccctg aacccagtc 60
ctgcagccat ggctcccggc cagctcgctt tatttagtgt ctctgacaaa accggccttg 120
tggaatttgc aagaaacctg accgctcttg gtttgaatct ggtcgcttcc ggagggactg 180
caaaagctct cagggatgct ggtctggcag tcagagatgt ctctgagttg acgggatttc 240
ctgaaatgtt ggggggacgt gtgaaaactt tgcctcctgc agtccatgct ggaatcctag 300
ctcgtaatat tcagaaagat aatgctgaca tggccagact tgatttcaat ctataagag 360
ttgttgctcg caatctctat ccctttgtaa agacagtggtc ttctccaggtg gtaagtgttg 420
agg 423

```

```

<210> 408
<211> 424
<212> DNA
<213> Homo sapiens

```

```

<400> 408
gaaaaaaaat agcttactga attctataag atgtgtggga atctcaccta tcaaaaaatag 60
gtaaaaagag cctccaaacc ctctcttgatt ttattcaact attcttttag gccagggaact 120
aatttaccct tcactatcct gttccctctt gctatcttgt ggagctctta aagacaaagg 180
tataaagacg ttttggtagg tgaattaata atcaactaga tggcatttcc aaatgggagt 240
gcacatactg tggggcaagt cccaagtga cttcaaaagt agacgtttat ttgagtatc 300
cttcagatgt aacaataatc ataatagcag ttaccacttc ctgagtagct tctatatgcc 360
atgtattgag ctgtgctcact tctttatgtg gattcttatt taactttaat accaagatga 420
ggtg 424

```

```

<210> 409
<211> 398
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(398)
<223> n = A,T,C or G

```

```

<400> 409
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tgtccagatt ggcaatgcct gctggggagct ctactgcctg gaacacggca tccagccgca 180
tgccagatcg ccaagtgcac agaccattgg gggaggagat gactccttca acacctctt 240
cagtgagacg ggcgctggca agcagctgcc cggggctgng tttgtagact tggaaaccac 300
agtnattgat gaagntcgna ctggcaccta cccgcaggtc ttncaccctg ancanntcat 360
nacaggcaag gaagatgctg ncaataaact atgccgca 398

```

```

<210> 410
<211> 423
<212> DNA
<213> Homo sapiens

```

```

<400> 410
gccccacccc acctgcccgc tgcggctctc cgcgggagat ctcaccgttc tggagacag 60
gctcgctcgc tctcacgtgc cccggccagc ccgcttctct gcccgagcgc atgaatctca 120
gtacgcccag tagcacggag gaaaaggcag tgacgaccgt gctctggggc tgcgagctca 180
gtcaggagag gcggacttgg accttcagac ccagctgga ggggaagcag agctgcaggc 240
tgttgcttca tacgatttgc ttgggggaga aagccaaaga ggagatgcac cgcgtggaga 300
tcttgcctcc agcaaacccag gaggacaaga agatgcagcc ggctaccatt gcctcactcc 360
aggctcagtc cctcccatg gtctccatgg taggagtgc gctttctccc ccagtctact 420
tcc 423

```

```

<210> 411
<211> 424
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(424)
<223> n = A,T,C or G

```

```

<400> 411
gcgaggcgca ctagcgccgg cgaggagcgg gccgagaggg cgtgcgggac gcggggcgcca 60
ggaccggcgc aacgcagagc ttgattcttc accacactga aaccattagg aaaaatcctt 120
gtggttaaca gcagaggctt cagagtgtaa cctgtactcg ggcctagaata ttatttataaa 180
tggcgactga tacgtctcaa ggtgaactcg tccatcctaa ggcactccca cttatagtag 240
gagctcagct gatccacgcg gacaagttag gtgagaaggt agaagatagc accatgccga 300
ttcgtcgaac tgtgaattct acccgggaaa ctctcccaa aagcaagctt gctgaagggc 360
aggaagaaan gccagaaaca gacataagtt cagaggaatc tgtctccact gtagaagaac 420
aaga 424

```

```

<210> 412
<211> 430
<212> DNA
<213> Homo sapiens

```

```

<400> 412
ggcacgaggt gaagccggcg ccagttccgg gggtccgggg ccgccactca gagctatgag 60
ctacggccgc cccctctccc atgtggaggg tatgacctcc ctcaaagggtg acaacctgac 120
ctaccgcacc tcgcccgaca cgtcgaggcg cgtcttcgag aagtacgggc gcgtcggcga 180
cgtgtacatc ccgcggggtc gctacaccaa ggatcccgcc ggcttcgact tgcctcgctt 240
tcacgacaag cgcgacgctg aggacgctat ggatgccatg gacggggccg tgcgtggacg 300
ccgcgagctg cgggtgcgca ttggcgcgcta cggccgcccc ccggaactcac accacagccg 360
ccgggggaccg ccaccccgca ggtacggggg cggtggtctac ggacgccgga gccgcagccc 420
taggcgcgct 430

```

```

<210> 413
<211> 429
<212> DNA
<213> Homo sapiens

```

```

<400> 413
ggcacgaggt cggcccgccc atcttgtggg aagagctgaa gcaggcgctc ttggctcggc 60
gcggcccgct gcaatccgtg gaggaaacgc ccgccagacc accatcatgc ctggggcactt 120
acaggaaagg ttcggctcgc tggtcaccaa ccgattcgac cagttatttt acgacgaate 180
ggaccacctc gaggtgctga aggcagcaga gaacaagaaa aaagaagccg gcggggggcg 240
cgttgggggc cctggggcca agagcgcagc tcaggcccgcg gccacagaca actccaacgc 300
ggcaggcaaa cagctgcgca aggagtccta gaaagaccgc aagaaccgcg tgccccccag 360
cgttggcgctg gttgacaaga aagaggagac gcagccgccc gtggcgctta agaaaagag 420

```

```

aataagacg                                     429

<210> 414
<211> 429
<212> DNA
<213> Homo sapiens

<400> 414
ggcacgagga cgggcccgcc tgccggcccc cgctctgccc tgcataataa aatggctaat 60
cagggtgaatg gtaatcggtg acagttaaaa gaagagggaag aaccaatgga tacttccagt 120
gtaactcaca cagaacacta caagacactg atagaggcag gcctcccaca gaaggtggca 180
gaaagacttg atgaaatatt tcagacagga ttggtagctt atgtcgatct tgatgaaaga 240
gcaattgatg ctctcaggga atttaatgaa gaaggagctc tgtctgtact acagcagttc 300
aaggaaagtg acttatcaca tgttcagaac aaaagtgcat ttttatgtgg agttatgaag 360
acctacaggc agagagagaa acagggggagc aaggtgcaag agtccacaaa gggacctgat 420
gaagcgaa                                         429

<210> 415
<211> 398
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(398)
<223> n = A,T,C or G

<400> 415
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cgctctcgcc gaggacaacag tcggtcagga agcccgcgcg caacagccat ggcttttaag 120
gataccggaa aaacaccctg ggagccggag gtggcaattc accgaattcg aatcaccccta 180
acaagccgca acgtaaaatc cttggaaaag gtgtgtgctg acttgataag aggcgcacaaa 240
gaaaagaatc tcaaaagtact ttgagaatca ctacaagaaa aactccttgt ggtgaaggtt 300
ctaagacgtg ggatcggttc cagatgagaa ttcacaagcg actcattgac ttgcacagtc 360
ctctcgagat tgttaagcan attacttcca tcantatt                                         398

<210> 416
<211> 269
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(269)
<223> n = A,T,C or G

<400> 416
gccgagggcag gaagctgtga gtgcgcggtt gcgggggtgc atttgtgcta cggcttttgc 60
tcccgcggcg gcagcccagc gctgggtccc gcctccgctc tccccaccgg cggggaaaagc 120
agctgtgtgt ggaggaaaag ctccatcccc cgccccctct ctcccgtgtg ttgctggcan 180
gatcttttgg cagtctctgt gnetcnctcc ccgncgggat cctnctgacc ctganattcn 240
nggtntnacc nnccgtnacc gccttgntt                                         269

<210> 417
<211> 408
<212> DNA
<213> Homo sapiens

```

<400> 417  
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 ggagcctctt gcaggataaa cagcagctag aggagctggc acggcaggcc gtggaccggg 120  
 ccttggtgta gggagtattg ctgaggacct cacaggagcc cacttcctcg gaggtggtga 180  
 gctatgcccc attcacgctc ttccctccac tgggtcccgag tgccctgctg gagcaagcct 240  
 atgctgtgca gatggaactc aaactgctag tggatgctgt cagccagaaac gctgacctcc 300  
 tggagcaaac ttcttccagc accatcaaac aggatgactt taccgctcgt ctctttgaca 360  
 tcacaagca agtcctaaaa gagggcattg cccagactgt gttcctcg 408

<210> 418  
 <211> 402  
 <212> DNA  
 <213> Homo sapiens

<400> 418  
 gagccgggga gccgcttccc gcccccgagc aggagccggt gcgagcggag cagagccgag 60  
 gtcggggcgc gagcggagcc ggctgagcgg gcgcccagct cccgccatgg ccggaacac 120  
 gctgtcctcg cgcttcgcc ggttgacat cgacgaattt gacgagaaca aatttggtga 180  
 cgagcaggag gagggcgccg cggcgccggc ggagccaggg ccggaccoga gcgaggtgga 240  
 cgggctcctg cggcaagggg acatgcttcg ggcatccat gcagccttgc gaaactctcc 300  
 cgtcaacacc aagaatcaag ctgtgaagga gcgagccag ggctgggtgc tgaagtgt 360  
 caaaaacttc aagagcagtg agattgagca ggctgtgcag tc 402

<210> 419  
 <211> 406  
 <212> DNA  
 <213> Homo sapiens

<400> 419  
 gccggggtca gcggcctggg ttgggctttg tagctgtctc gcaggccag cccggggcgc 60  
 gctcgagagc tcttaggcgg tgcggcgctt cctgcctcct cctctctcgg cgtgctgggc 120  
 ccgcccggct ccgcggtgcc tgccttcgct ctcaggttga ggagctcaag cttgggaaaa 180  
 tgggtgtcat tctctgtatc gtcattccag ttctgtctg gatctacaaa aaattcctgg 240  
 agccatatac ataccctctg gtttccctct tctgtaagtc gtatatggcc taaaaaaga 300  
 attcaaaaga atccaatgat ccaaacaaaa gggcaaaagt aaaaactttt aaagggtgtc 360  
 aagaacattg aaatgggaat tacccaacca aaaaagggaa cccaac 406

<210> 420  
 <211> 371  
 <212> DNA  
 <213> Homo sapiens

<400> 420  
 cagccatcgt ggtgtgttct tgactccgct gctcgccatg tctttctaca agactttcag 60  
 gattaaagca ttctctggcca agaaacaaaa gcaaaatcgt cccattcccc agtggattcg 120  
 gatgaatact gaaataaaaa tcagggtacaa ctccaaaagg agacattgga gaagaaccaa 180  
 gctgggtctc taagggaatt cacatgagat gccacacata ttatgtgtgt ctgaagggtca 240  
 cgatcatggt accatatcaa gctgaaaaat tcaccaactat ctggagattt cgacgtgttt 300  
 tctctctcta atctgttatg aacacgttgg ttggtgggat tcagtaataa atatgtaagg 360  
 cctttctttt t 371

<210> 421  
 <211> 51  
 <212> PRT  
 <213> Homo sapiens

<400> 421

[illegible]

```
<210> 422
<211> 12308
<212> DNA
<213> Homo sapiens
```

[illegible]

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gtgtttgttaa	agccacaaga	tcacactcct	cctccagccc	catcccgagc	tcocatccag	2760
gatagtcttt	ctcaggctca	gactctctcag	ccacccctcac	cgcaagtgtt	ttcacctggg	2820
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ccatccctgt	tcagagattt	atgttctctc	tcacagacaa	ataatgcacc	ctatgcaaaa	3060
cctccagaca	caactaggcc	tgtgatgaca	gatcaatttc	ccaaatcctt	ggccctatcc	3120
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gacccactgc	gacgacctcc	ccagggtcta	ctctaactcag	tacctgtgca	ccagattttg	5040
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&lt;210&gt; 423

&lt;211&gt; 596

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 423

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ccgccatttg tgtccttggc caggaccocg agaaccagcg gctgctcagg ttttactgt 180
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&lt;210&gt; 424

&lt;211&gt; 1549

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 424

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&lt;210&gt; 425

&lt;211&gt; 4019

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 425

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Val Cys Gly Ser Phe Gly Gln Gly Ala Glu Gly Arg Leu Leu Ala Cys
                    20              25              30
Ser Gln Cys Gly Gln Cys Tyr His Pro Tyr Cys Val Ser Ile Lys Ile
                    35              40              45
Thr Lys Val Val Leu Ser Lys Gly Trp Arg Cys Leu Glu Cys Thr Val
                    50              55              60
Cys Glu Ala Cys Gly Lys Ala Thr Asp Pro Gly Arg Leu Leu Leu Cys
                    65              70              75
Asp Asp Cys Asp Ile Ser Tyr His Thr Tyr Cys Leu Asp Pro Pro Leu
                    80              85              90              95

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 Arg His Cys Gly Ala Thr Ser Ala Gly Leu Arg Cys Glu Trp Gln Asn  
 115 120 125  
 Asn Tyr Thr Gln Cys Ala Pro Cys Ala Ser Leu Ser Cys Pro Val  
 130 135 140  
 Cys Tyr Arg Asn Tyr Arg Glu Glu Asp Leu Ile Leu Gln Cys Arg Gln  
 145 150 155 160  
 Cys Asp Arg Trp Met His Ala Val Cys Gln Asn Leu Asn Thr Glu Glu  
 165 170 175  
 Glu Val Glu Asn Val Ala Asp Ile Gly Phe Asp Cys Ser Met Cys Arg  
 180 185 190  
 Pro Tyr Met Pro Ala Ser Asn Val Pro Ser Ser Asp Cys Cys Glu Ser  
 195 200 205  
 Ser Leu Val Ala Gln Ile Val Thr Lys Val Lys Glu Leu Asp Pro Pro  
 210 215 220  
 Lys Thr Tyr Thr Gln Asp Gly Val Cys Leu Thr Glu Ser Gly Met Thr  
 225 230 235 240  
 Gln Leu Gln Ser Leu Thr Val Thr Val Pro Arg Arg Lys Arg Ser Lys  
 245 250 255  
 Pro Lys Leu Lys Leu Lys Ile Ile Asn Gln Asn Ser Val Ala Val Leu  
 260 265 270  
 Gln Thr Pro Pro Asp Ile Gln Ser Glu His Ser Arg Asp Gly Glu Met  
 275 280 285  
 Asp Asp Ser Arg Glu Gly Glu Leu Met Asp Cys Asp Gly Lys Ser Glu  
 290 295 300  
 Ser Ser Pro Glu Arg Glu Ala Val Asp Asp Glu Thr Lys Gly Val Glu  
 305 310 315 320  
 Gly Thr Asp Gly Val Lys Lys Arg Lys Arg Lys Pro Tyr Arg Pro Gly  
 325 330 335  
 Ile Gly Gly Phe Met Val Arg Gln Arg Ser Arg Thr Gly Gln Gly Lys  
 340 345 350  
 Thr Lys Arg Ser Val Ile Arg Lys Asp Ser Ser Gly Ser Ile Ser Glu  
 355 360 365  
 Gln Leu Pro Cys Arg Asp Asp Gly Trp Ser Glu Gln Leu Pro Asp Thr  
 370 375 380  
 Leu Val Asp Glu Ser Val Ser Val Thr Glu Ser Thr Glu Lys Ile Lys  
 385 390 395 400  
 Lys Arg Tyr Arg Lys Arg Lys Asn Lys Leu Glu Glu Thr Phe Pro Ala  
 405 410 415  
 Tyr Leu Gln Glu Ala Phe Phe Gly Lys Asp Leu Leu Asp Thr Ser Arg  
 420 425 430  
 Gln Ser Lys Ile Ser Leu Asp Asn Leu Ser Glu Asp Gly Ala Gln Leu  
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 Leu Tyr Lys Thr Asn Met Asn Thr Gly Phe Leu Asp Pro Ser Leu Asp  
 450 455 460  
 Pro Leu Leu Ser Ser Ser Ser Ala Pro Thr Lys Ser Gly Thr His Gly  
 465 470 475 480  
 Pro Ala Asp Asp Pro Leu Ala Asp Ile Ser Glu Val Leu Asn Thr Asp  
 485 490 495  
 Asp Asp Ile Leu Gly Ile Ile Ser Asp Asp Leu Ala Lys Ser Val Asp  
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 His Ser Asp Ile Gly Pro Val Thr Asp Asp Pro Ser Ser Leu Pro Gln  
 515 520 525  
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 530 535 540  
 Gly Ile Leu Ser Pro Glu Leu Asp Lys Met Val Thr Asp Gly Ala Ile  
 545 550 555 560

Leu Gly Lys Leu Tyr Lys Ile Pro Glu Leu Gly Gly Lys Asp Val Glu  
 565 570 575  
 Asp Leu Phe Thr Ala Val Leu Ser Pro Ala Asn Thr Gln Pro Thr Pro  
 580 585 590  
 Leu Pro Gln Pro Pro Pro Thr Gln Leu Leu Pro Ile His Asn Gln  
 595 600 605  
 Asp Ala Phe Ser Arg Met Pro Leu Met Asn Gly Leu Ile Gly Ser Ser  
 610 615 620  
 Pro His Leu Pro His Asn Ser Leu Pro Pro Gly Ser Gly Leu Gly Thr  
 625 630 635 640  
 Phe Ser Ala Ile Ala Gln Ser Ser Tyr Pro Asp Ala Arg Asp Lys Asn  
 645 650 655  
 Ser Ala Phe Asn Pro Met Ala Ser Asp Pro Asn Asn Ser Trp Thr Ser  
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 740 745 750  
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 Lys Gln Gln Ala Lys Ile Glu Ala Thr Gln Lys Leu Glu Gln Val Lys  
 820 825 830  
 Asn Glu Gln Gln Gln Gln Gln Gln Phe Gly Ser Gln His Leu  
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 Leu Val Gln Ser Gly Ser Asp Thr Pro Ser Ser Gly Ile Gln Ser Pro  
 850 855 860  
 Leu Thr Pro Gln Pro Gly Asn Gly Asn Met Ser Pro Ala Gln Ser Phe  
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 His Lys Glu Leu Phe Thr Lys Gln Pro Pro Ser Thr Pro Thr Ser Thr  
 885 890 895  
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 930 935 940  
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 945 950 955 960  
 Arg Pro Pro Pro Val Gly His Ser Phe Ser Arg Arg Asn Ser Ala Ala  
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 Pro Val Glu Asn Cys Thr Pro Leu Ser Ser Val Ser Arg Pro Leu Gln  
 980 985 990  
 Met Asn Glu Thr Thr Ala Asn Arg Pro Ser Pro Val Arg Asp Leu Cys  
 995 1000 1005  
 Ser Ser Ser Thr Thr Asn Asn Asp Pro Tyr Ala Lys Pro Pro Asp Thr  
 1010 1015 1020

Pro Arg Pro Val Met Thr Asp Gln Phe Pro Lys Ser Leu Gly Leu Ser  
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 1090 1095 1100  
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 1490 1495 1500  
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 Tyr Pro Pro Asp Val Ala Ser Met Gly Met Arg Pro His Gly Phe Arg  
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 Phe Leu Val Pro Pro Gln Gln Ile Gln Gly Ser Gly Val Ser Pro Gln  
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 Lys Ser Met Phe Asn Glu Glu Leu Asp Leu Pro Ile Asp Asp Lys Leu  
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 1955 1960 1965  
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 1970 1975 1980  
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 1985 1990 1995 2000  
 Ser Pro Ser Asn His Val Ser Ser Leu Pro Pro Phe Ile Ala Pro Pro  
 2005 2010 2015  
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&lt;211&gt; 174

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 426

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 Pro Glu Asn Gln Ala Leu Ala Arg Phe Tyr Cys Tyr Thr Glu Arg Thr  
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 Leu Trp Gly Asp Arg Pro Glu Ala Gln Leu Gly Ser Gln Ala Asp Ser  
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&lt;210&gt; 429

&lt;211&gt; 732

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 429

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&lt;210&gt; 430

&lt;211&gt; 2843

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 430

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&lt;210&gt; 431

&lt;211&gt; 640

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 431

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&lt;210&gt; 432

&lt;211&gt; D68

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 432

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&lt;210&gt; 433

&lt;211&gt; 1723

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 433

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&lt;210&gt; 434

&lt;211&gt; 1702

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 434

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Val Asp Gly Ile Tyr Arg Leu Ser Gly Val Ala Ser Asn Ile Gln Arg
                    20                25                30
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                    35                40                45
Pro Tyr Val Gln Asp Ile His Ser Val Gly Ser Leu Cys Lys Leu Tyr
                    50                55                60
Phe Arg Glu Leu Pro Asn Pro Leu Leu Thr Tyr Gln Leu Tyr Glu Lys
                    65                70                75                80
Phe Ser Asp Ala Val Ser Ala Ala Thr Asp Glu Glu Arg Leu Ile Lys
                    85                90                95
Ile His Asp Val Ile Gln Gln Leu Pro Pro Pro His Tyr Arg Thr Leu
                    100                105                110
Glu Phe Leu Met Arg His Leu Ser Leu Leu Ala Asp Tyr Cys Ser Ile
                    115                120                125
Thr Asn Met His Ala Lys Asn Leu Ala Ile Val Trp Ala Pro Asn Leu
                    130                135                140
Leu Arg Ser Lys Gln Ile Glu Ser Ala Cys Phe Ser Gly Thr Ala Ala
                    145                150                155                160
Phe Met Glu Val Arg Ile Gln Ser Val Val Val Glu Phe Ile Leu Asn
                    165                170                175
His Val Asp Val Leu Phe Ser Gly Arg Ile Ser Met Ala Met Gln Glu

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Gly	Ser	Trp	Arg	Ser	Phe	Phe	Asn	Leu	Gly	Lys	Ser	Ser	Ser	Val	Ser
		275					280								
Lys	Arg	Lys	Leu	Gln	Arg	Asn	Glu	Ser	Glu	Pro	Ser	Glu	Met	Lys	Ala
		290					295					300			
Met	Ala	Leu	Lys	Gly	Gly	Arg	Ala	Glu	Gly	Thr	Leu	Arg	Ser	Ala	Lys
		305					310				315				320
Ser	Glu	Glu	Ser	Leu	Thr	Ser	Leu	His	Ala	Val	Asp	Gly	Asp	Ser	Lys
							325								335
Leu	Phe	Arg	Pro	Arg	Arg	Pro	Arg	Ser	Ser	Ser	Asp	Ala	Leu	Ser	Ala
							340								350
Ser	Phe	Asn	Gly	Glu	Met	Leu	Gly	Asn	Arg	Cys	Asn	Ser	Tyr	Asp	Asn
		355					360					365			
Leu	Pro	His	Asp	Asn	Glu	Ser	Glu	Glu	Gly	Gly	Leu	Leu	His	Ile	
		370					375					380			
Pro	Ala	Leu	Met	Ser	Pro	His	Ser	Ala	Glu	Asp	Val	Asp	Leu	Ser	Pro
		385					390				395				400
Pro	Asp	Ile	Gly	Val	Ala	Ser	Leu	Asp	Phe	Asp	Pro	Met	Ser	Phe	Gln
							405								415
Cys	Ser	Pro	Pro	Lys	Ala	Glu	Ser	Glu	Cys	Leu	Glu	Ser	Gly	Ala	Ser
							420								430
Phe	Leu	Asp	Ser	Pro	Gly	Tyr	Ser	Lys	Asp	Lys	Pro	Ser	Ala	Asn	Lys
		435					440								445
Lys	Asp	Ala	Glu	Thr	Gly	Ser	Ser	Gln	Cys	Gln	Thr	Pro	Gly	Ser	Thr
		450					455					460			
Ala	Ser	Ser	Glu	Pro	Val	Ser	Pro	Leu	Gln	Glu	Lys	Leu	Ser	Pro	Phe
		465					470				475				480
Phe	Thr	Leu	Asp	Leu	Ser	Pro	Thr	Glu	Asp	Lys	Ser	Ser	Lys	Pro	Ser
							485								495
Ser	Phe	Thr	Glu	Lys	Val	Val	Tyr	Ala	Phe	Ser	Pro	Lys	Ile	Gly	Arg
							500								510
Lys	Leu	Ser	Lys	Ser	Pro	Ser	Met	Ser	Ile	Ser	Glu	Pro	Ile	Ser	Val
		515					520								525
Thr	Leu	Pro	Pro	Arg	Val	Ser	Glu	Val	Ile	Gly	Thr	Val	Ser	Asn	Thr
		530					535					540			
Thr	Ala	Gln	Asn	Ala	Ser	Ser	Ser	Thr	Trp	Asp	Lys	Cys	Val	Glu	Glu
		545					550				555				560
Arg	Asp	Ala	Thr	Asn	Arg	Ser	Pro	Thr	Gln	Ile	Val	Lys	Met	Lys	Thr
							565								575
Asn	Glu	Thr	Val	Ala	Gln	Glu	Ala	Tyr	Glu	Ser	Glu	Val	Gln	Pro	Leu
		580							585						590
Asp	Gln	Val	Ala	Ala	Glu	Glu	Val	Glu	Leu	Pro	Gly	Lys	Glu	Asp	Gln
		595					600					605			
Ser	Val	Ser	Ser	Ser	Gln	Ser	Lys	Ala	Val	Ala	Ser	Gly	Gln	Thr	Gln
		610					615					620			
Thr	Gly	Ala	Val	Thr	His	Asp	Pro	Pro	Gln	Asp	Ser	Val	Pro	Val	Ser
		625					630					635			640
Ser	Val	Ser	Leu	Ile	Pro	Pro	Pro	Pro	Pro	Pro	Lys	Asn	Val	Ala	Arg

Met	Leu	Ala	Leu	Ala	Leu	Ala	Glu	Ser	Ala	Gln	Gln	Ala	Ser	Thr	Gln	
Ser	Leu	Lys	Arg	Pro	Gly	Thr	Ser	Gln	Ala	Gly	Tyr	Thr	Asn	Tyr	Gly	
Asp	Ile	Ala	Val	Ala	Thr	Thr	Glu	Asp	Asn	Leu	Ser	Ser	Ser	Tyr	Ser	
Ala	Val	Ala	Leu	Asp	Lys	Ala	Tyr	Phe	Gln	Thr	Asp	Arg	Pro	Ala	Glu	
Gln	Phe	His	Leu	Gln	Asn	Asn	Ala	Pro	Gly	Asn	Cys	Asp	His	Pro	Leu	
Pro	Glu	Thr	Thr	Ala	Thr	Gly	Asp	Pro	Thr	His	Ser	Asn	Thr	Thr	Glu	
Ser	Gly	Glu	Gln	His	His	Gln	Val	Asp	Leu	Thr	Gly	Asn	Gln	Pro	His	
Gln	Ala	Tyr	Leu	Ser	Gly	Asp	Pro	Glu	Lys	Ala	Arg	Ile	Thr	Ser	Val	
Pro	Leu	Asp	Ser	Glu	Lys	Ser	Asp	Asp	His	Val	Ser	Phe	Pro	Glu	Asp	
Gln	Ser	Gly	Lys	Asn	Ser	Met	Pro	Thr	Val	Ser	Phe	Leu	Asp	Gln	Asp	
Gln	Ser	Pro	Pro	Arg	Phe	Tyr	Ser	Gly	Asp	Gln	Pro	Pro	Ser	Tyr	Leu	
Gly	Ala	Ser	Val	Asp	Lys	Leu	His	His	Pro	Leu	Glu	Phe	Ala	Asp	Lys	
Ser	Pro	Thr	Pro	Pro	Asn	Leu	Pro	Ser	Asp	Lys	Ile	Tyr	Pro	Pro	Ser	
Gly	Ser	Pro	Glu	Glu	Asn	Thr	Ser	Thr	Ala	Thr	Met	Thr	Tyr	Met	Thr	
Thr	Thr	Pro	Ala	Thr	Ala	Gln	Met	Ser	Thr	Lys	Glu	Ala	Ser	Trp	Asp	
Val	Ala	Glu	Gln	Pro	Thr	Thr	Ala	Asp	Phe	Ala	Ala	Ala	Thr	Leu	Gln	
Arg	Thr	His	Arg	Thr	Asn	Arg	Pro	Leu	Pro	Pro	Pro	Pro	Ser	Gln	Arg	
Ser	Ala	Glu	Gln	Pro	Pro	Val	Val	Gly	Gln	Val	Gln	Ala	Ala	Thr	Asn	
Ile	Gly	Leu	Asn	Asn	Ser	His	Lys	Val	Gln	Gly	Val	Val	Pro	Val	Pro	
Glu	Arg	Pro	Pro	Glu	Pro	Arg	Ala	Met	Asp	Asp	Pro	Ala	Ser	Ala	Phe	
Ile	Ser	Asp	Ser	Gly	Ala	Ala	Ala	Ala	Gln	Cys	Pro	Met	Ala	Thr	Ala	
Val	Gln	Pro	Gly	Leu	Pro	Glu	Lys	Val	Arg	Asp	Gly	Ala	Arg	Val	Pro	
Leu	Leu	His	Leu	Arg	Ala	Glu	Ser	Val	Pro	Ala	His	Pro	Cys	Gly	Phe	
Pro	Ala	Pro	Leu	Pro	Pro	Thr	Arg	Met	Met	Glu	Ser	Lys	Met	Ile	Ala	
Ala	Ile	His	Ser	Ser	Ser	Ala	Asp	Ala	Thr	Ser	Ser	Ser	Asn	Tyr	His	
Ser	Phe	Val	Thr	Ala	Ser	Ser	Thr	Ser	Val	Asp	Asp	Ala	Leu	Pro	Leu	
Pro	Leu	Pro	Val	Pro	Gln	Pro	Lys	His	Ala	Ser	Gln	Lys	Thr	Val	Tyr	
Ser	Ser	Phe	Ala	Arg	Pro	Asp	Val	Thr	Thr	Glu	Pro	Phe	Gly	Pro	Asp	
Asn	Cys	Leu	His	Phe	Asn	Met	Thr	Pro	Asn	Cys	Gln	Tyr	Arg	Pro	Gln	

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1570                      1575                      1580  
 Glu Glu His Leu Thr Gln Ser Ile Val Pro Pro Pro Lys Pro Glu Arg  
 1585                      1590                      1595                      1600  
 Ser His Ser Leu Lys Leu His His Thr Gln Asn Val Glu Arg Asp Pro  
                     1605                      1610                      1615  
 Ser Val Leu Tyr Gln Tyr Gln Pro His Gly Lys Arg Gln Ser Ser Val  
                     1620                      1625                      1630  
 Thr Val Val Ser Gln Tyr Asp Asn Leu Glu Asp Tyr His Ser Leu Pro  
                     1635                      1640                      1645  
 Gln His Gln Arg Gly Val Phe Gly Gly Gly Met Gly Thr Tyr Val  
                     1650                      1655                      1660  
 Pro Pro Gly Phe Pro His Pro Gln Ser Arg Thr Tyr Ala Thr Ala Leu  
 1665                      1670                      1675                      1680  
 Gly Gln Gly Ala Phe Leu Pro Ala Glu Leu Ser Leu Gln His Pro Glu  
                     1685                      1690                      1695  
 Thr Gln Ile His Ala Glu  
                     1700

<210> 435  
 <211> 160  
 <212> PRT  
 <213> Homo sapiens

<400> 435  
 Pro Phe Gln Gln Val Gly Arg Cys Asn Pro Ser Pro Gln Thr Arg Pro  
                     5                      10                      15  
 Gly Pro Ala Ser Lys Val Lys Gln Asp Met Pro Pro Pro Gly Gly Tyr  
                     20                      25                      30  
 Gly Pro Ile Asp Tyr Lys Arg Asn Leu Pro Arg Arg Gly Leu Ser Gly  
                     35                      40                      45  
 Tyr Ser Met Leu Ala Ile Gly Ile Gly Thr Leu Ile Tyr Gly His Trp  
                     50                      55                      60  
 Ser Ile Met Lys Trp Asn Arg Glu Arg Arg Arg Leu Gln Ile Glu Asp  
 65                      70                      75                      80  
 Phe Glu Ala Arg Ile Ala Leu Leu Pro Leu Leu Gln Ala Glu Thr Asp  
                     85                      90                      95  
 Arg Arg Thr Leu Gln Met Leu Arg Glu Asn Leu Glu Glu Ala Ile  
                     100                      105                      110  
 Ile Met Lys Asp Val Pro Asp Trp Lys Val Gly Glu Ser Val Phe His  
                     115                      120                      125  
 Thr Thr Arg Trp Val Pro Pro Leu Ile Gly Glu Leu Tyr Gly Leu Arg  
                     130                      135                      140  
 Thr Thr Glu Glu Ala Leu His Ala Ser His Gly Phe Met Trp Tyr Thr  
 145                      150                      155                      160

<210> 436  
 <211> 396  
 <212> PRT  
 <213> Homo sapiens

<400> 436  
 Arg Ala Gln Glu Ala Ala Ala Ala Ala Ala Asp Gly Pro Pro Ala Ala  
                     5                      10                      15  
 Asp Gly Glu Asp Gly Gln Asp Pro His Ser Lys His Leu Tyr Thr Ala  
                     20                      25                      30  
 Asp Met Phe Thr His Gly Ile Gln Ser Ala Ala His Phe Val Met Phe

35 40 45  
 Phe Ala Pro Trp Cys Gly His Cys Gln Arg Leu Gln Pro Thr Trp Asn  
 50 55 60  
 Asp Leu Gly Asp Lys Tyr Asn Ser Met Glu Asp Ala Lys Val Tyr Val  
 65 70 75 80  
 Ala Lys Val Asp Cys Thr Ala His Ser Asp Val Cys Ser Ala Gln Gly  
 85 90 95  
 Val Arg Gly Tyr Pro Thr Leu Lys Leu Phe Lys Pro Gly Gln Glu Ala  
 100 105 110  
 Val Lys Tyr Gln Gly Pro Arg Asp Phe Gln Thr Leu Glu Asn Trp Met  
 115 120 125  
 Leu Gln Thr Leu Asn Glu Glu Pro Val Thr Pro Glu Pro Glu Val Glu  
 130 135 140  
 Pro Pro Ser Ala Pro Glu Leu Lys Gln Gly Leu Tyr Glu Leu Ser Ala  
 145 150 155 160  
 Ser Asn Phe Glu Leu His Val Ala Gln Gly Asp His Phe Ile Lys Phe  
 165 170 175  
 Phe Ala Pro Trp Cys Gly His Cys Lys Ala Leu Ala Pro Thr Trp Glu  
 180 185 190  
 Gln Leu Ala Leu Gly Leu Glu His Ser Glu Thr Val Lys Ile Gly Lys  
 195 200 205  
 Val Asp Cys Thr Gln His Tyr Glu Leu Cys Ser Gly Asn Gln Val Arg  
 210 215 220  
 Gly Tyr Pro Thr Leu Leu Trp Phe Arg Asp Gly Lys Lys Val Asp Gln  
 225 230 235 240  
 Tyr Lys Gly Lys Arg Asp Leu Glu Ser Leu Arg Glu Tyr Val Glu Ser  
 245 250 255  
 Gln Leu Gln Arg Thr Glu Thr Gly Ala Thr Glu Thr Val Thr Pro Ser  
 260 265 270  
 Glu Ala Pro Val Leu Ala Ala Glu Pro Glu Ala Asp Lys Gly Thr Val  
 275 280 285  
 Leu Ala Leu Thr Glu Asn Thr Phe Asp Asp Thr Ile Ala Glu Gly Ile  
 290 295 300  
 Thr Phe Ile Lys Phe Tyr Ala Pro Trp Cys Gly His Cys Lys Thr Leu  
 305 310 315 320  
 Ala Pro Thr Trp Glu Glu Leu Ser Lys Lys Glu Phe Pro Gly Leu Ala  
 325 330 335  
 Gly Val Lys Ile Ala Glu Val Asp Cys Thr Ala Glu Arg Asn Ile Cys  
 340 345 350  
 Ser Lys Tyr Ser Val Arg Gly Tyr Pro Thr Leu Leu Leu Phe Arg Gly  
 355 360 365  
 Gly Lys Lys Val Ser Glu His Ser Gly Gly Arg Asp Leu Asp Ser Leu  
 370 375 380  
 His Arg Phe Val Leu Ser Gln Ala Lys Asp Glu Leu  
 385 390 395

&lt;210&gt; 437

&lt;211&gt; 92

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

Ala Glu Met Asp Pro Leu Arg Ala Gln Gln Leu Ala Ala Glu Leu Glu  
 5 10 15  
 Val Glu Met Met Ala Asp Met Tyr Asn Arg Met Thr Ser Ala Cys His  
 20 25 30  
 Arg Lys Cys Val Pro Pro His Tyr Lys Glu Ala Glu Leu Ser Lys Gly

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      35              40              45
Glu Ser Val Cys Leu Asp Arg Cys Val Ser Lys Tyr Leu Asp Ile His
   50              55              60
Glu Arg Met Gly Lys Lys Leu Thr Glu Leu Ser Met Gln Asp Glu Glu
   65              70              75
Leu Met Lys Arg Val Gln Gln Ser Ser Gly Pro Ala
      85              90

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<210> 438  
 <211> 303  
 <212> PRT  
 <213> Homo sapiens

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<400> 438
Lys Asn Pro Ala Lys Met Ser Leu Tyr Pro Ser Leu Glu Asp Leu Lys
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Val Asp Lys Val Ile Gln Ala Gln Thr Ala Phe Ser Ala Asn Pro Ala
      20              25              30
Asn Pro Ala Ile Leu Ser Glu Ala Ser Ala Pro Ile Pro His Asp Gly
      35              40              45
Asn Leu Tyr Pro Arg Leu Tyr Pro Glu Leu Ser Gln Tyr Met Gly Leu
      50              55              60
Ser Leu Asn Glu Glu Glu Ile Arg Ala Asn Val Ala Val Val Ser Gly
      65              70              75
Ala Pro Leu Gln Gly Gln Leu Val Ala Arg Pro Ser Ser Ile Asn Tyr
      85              90              95
Met Val Ala Pro Val Thr Gly Asn Asp Val Gly Ile Arg Arg Ala Glu
      100              105              110
Ile Lys Gln Gly Ile Arg Glu Val Ile Leu Cys Lys Asp Gln Asp Gly
      115              120              125
Lys Ile Gly Leu Arg Leu Lys Ser Ile Asp Asn Gly Ile Phe Val Gln
      130              135              140
Leu Val Gln Ala Asn Ser Pro Ala Ser Leu Val Gly Leu Arg Phe Gly
      145              150              155
Asp Gln Val Leu Gln Ile Asn Gly Glu Asn Cys Ala Gly Trp Ser Ser
      165              170              175
Asp Lys Ala His Lys Val Leu Lys Gln Ala Phe Gly Glu Lys Ile Thr
      180              185              190
Met Thr Ile Arg Asp Arg Pro Phe Glu Arg Thr Ile Thr Met His Lys
      195              200              205
Asp Ser Thr Gly His Val Gly Phe Ile Phe Lys Asn Gly Lys Ile Thr
      210              215              220
Ser Ile Val Lys Asp Ser Ser Ala Ala Arg Asn Gly Leu Leu Thr Glu
      225              230              235
His Asn Ile Cys Glu Ile Asn Gly Gln Asn Val Ile Gly Leu Lys Asp
      245              250              255
Ser Gln Ile Ala Asp Ile Leu Ser Thr Ser Gly Thr Val Val Thr Ile
      260              265              270
Thr Ile Met Pro Ala Phe Ile Phe Glu His Ile Ile Lys Arg Met Ala
      275              280              285
Pro Ser Ile Met Lys Ser Leu Met Asp His Thr Ile Pro Glu Val
      290              295              300

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<210> 439  
 <211> 378  
 <212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 439

Val Val Pro Ser Thr Lys Asp Phe Leu Val Gly Val Lys Gly Ser Gly  
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 Gly His Arg Gly Gly Gly Glu Met Ala Phe Ser Gly Ser Gln Ala Pro  
 20 25 30  
 Tyr Leu Ser Pro Ala Val Pro Phe Ser Gly Thr Ile Gln Gly Gly Leu  
 35 40 45  
 Gln Asp Gly Leu Gln Ile Thr Val Asn Gly Thr Val Leu Ser Ser Ser  
 50 55 60  
 Gly Thr Arg Phe Ala Val Asn Phe Gln Thr Gly Phe Ser Gly Asn Asp  
 65 70 75 80  
 Ile Ala Phe His Phe Asn Pro Arg Phe Glu Asp Gly Gly Tyr Val Val  
 85 90 95  
 Cys Asn Thr Arg Gln Asn Gly Ser Trp Gly Pro Glu Glu Arg Lys Thr  
 100 105 110  
 His Met Pro Phe Gln Lys Gly Met Pro Phe Asp Leu Cys Phe Leu Val  
 115 120 125  
 Gln Ser Ser Asp Phe Lys Val Met Val Asn Gly Ile Leu Phe Val Gln  
 130 135 140  
 Tyr Phe His Arg Val Pro Phe His Arg Val Asp Thr Ile Ser Val Asn  
 145 150 155 160  
 Gly Ser Val Gln Leu Ser Tyr Ile Ser Phe Gln Asn Pro Arg Thr Val  
 165 170 175  
 Pro Val Gln Pro Ala Phe Ser Thr Val Pro Phe Ser Gln Pro Val Cys  
 180 185 190  
 Phe Pro Pro Arg Pro Arg Gly Arg Arg Gln Lys Pro Pro Gly Val Trp  
 195 200 205  
 Pro Ala Asn Pro Ala Pro Ile Thr Gln Thr Val Ile His Thr Val Gln  
 210 215 220  
 Ser Ala Pro Gly Gln Met Phe Ser Thr Pro Ala Ile Pro Pro Met Met  
 225 230 235 240  
 Tyr Pro His Pro Ala Tyr Pro Met Pro Phe Ile Thr Thr Ile Leu Gly  
 245 250 255  
 Gly Leu Tyr Pro Ser Lys Ser Ile Leu Leu Ser Gly Thr Val Leu Pro  
 260 265 270  
 Ser Ala Gln Arg Phe His Ile Asn Leu Cys Ser Gly Asn His Ile Ala  
 275 280 285  
 Phe His Leu Asn Pro Arg Phe Asp Glu Asn Ala Val Val Arg Asn Thr  
 290 295 300  
 Gln Ile Asp Asn Ser Trp Gly Ser Glu Glu Arg Ser Leu Pro Arg Lys  
 305 310 315 320  
 Met Pro Phe Val Arg Gly Gln Ser Phe Ser Val Trp Ile Leu Cys Glu  
 325 330 335  
 Ala His Cys Leu Lys Val Ala Val Asp Gly Gln His Leu Phe Glu Tyr  
 340 345 350  
 Tyr His Arg Leu Arg Asn Leu Pro Thr Ile Asn Arg Leu Glu Val Gly  
 355 360 365  
 Gly Asp Ile Gln Leu Thr His Val Gln Thr  
 370 375

&lt;210&gt; 440

&lt;211&gt; 2239

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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 catagatttt atcatattct gatttttttg gattcttttg ttttctcatc actggattca 180  
 ggaagcctgt ttgtgtccac catctccaaa ggaggttacc tgcagggaaa tgttaacggg 240  
 aggctgcctt cctctgggcaa caaggagcca cctgggcagg acgccttttc aggaagagac 300  
 gccttttcag gaagagacgc cttttcagga agagagaaag tgcagctgaa gaggaaagtc 360  
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 aagaaatctg gaggtcatta cacatatatt ttggaagtct ttggtccatt accagctttt 600  
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 ttgttaaagt ggttttacac actacagatg tctatactgt gaaaagtgtt ttaactctg 2160  
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 tattaataaa aaaaaaaaaa 2239

<210> 441  
 <211> 5981  
 <212> DNA  
 <213> Homo sapiens

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 tagattttat catattctat attttttgga ttcttttggt ttctcatcac tggattcagg 180  
 aaagcctgtt gtgtccacca tctccaaagg aggtttacct cagggaaatg ttaacgggag 240  
 gtgccttcca ctgggcaaca aggagccacc tgggcaggag aaagtgcagc tgaagaggaa 300  
 agtcaactta ctgaggggag tctccattat cattggcacc atgttgtag caggactctt 360  
 catctctcct aagggcctgc tccagaacac gggcagcgtg ggcagtctc tgaccattct 420  
 agcgtgtgtg ggggtcctgt cactatttgg actcttctat tgcgtgaat tgggaacaac 480  
 tataaagaaa tctggaggtc attacacata tattttggaa gtcttgggtc cattaccagc 540  
 tttttagaca gtctgggttg aactcctcat aatagcctct gacgtactg ctgtgatata 600



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tttattcata	tatttttagca	tattcgaact	aatttctaa	aaatttagtt	ataactctat	1860
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tttaaaataa ctaatatagt attttttaat ttttgtggg atggattctc aaatacttgt 4140
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aattacaatt tgacatatca atagagggtt aacaagagta taattacata acagaattcc 4620
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atataaaaat tagccgggag ttggtggcag cgcctgtaat ccagctactc cgggagctgt 5880
aggcaggaga atcacttgaa cccaaggggc agaagctgca gttagccaag atcgcatcat 5940
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```

&lt;210&gt; 442

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 442

```

gatggaggtt gaagt gagca gagatcatgc cagcctgggt gacagtgaga ctctgtctca 60
aacagaatta aggaaaaaa aaagaaagaa aaagagagag aggaaattcc aggccaatgt 120
tggcatagat ttatcataat tctggatttt ttggattttt ttgtttcttc atactggat 180
tcaggaaagc ctgttgtgtc caccatctcc aaaggaggtt acctgcaggg aaatgttaac 240
ggggaggtgc cttccctggg caacaaggag ccactctggc agggagaagt gcagctgaag 300
aggaaagcca cttacttag gggagtctcc attatca

```

&lt;210&gt; 443

&lt;211&gt; 739

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 443

```

gaattcgaac cccctcggat tctaatacag aaaaatgattt gctatgggaa gagaagtttc 60
ctgaaagaac aactgttact gaattacctc agacttcaca tgtatcattc tccgagctgt 120
atattccgtc ctcaaaaaat actgagttac ctgtggactgt gagtattaaa acgcgactcc 180
ttttcacctc ttctcaacc ctttactggc cagatcattt gaaagcagct gaagaagctc 240
aaggtcttgt ccagcattgt agggcaacag aagttacttt gcctaaaagt atacaggatc 300

```

```

ccaaactctc  ctctgagctc  cgttgtagct  tccagcagag  ccttatctat  tggctccacc  360
ctgctttgtc  ttgggtacca  ctgttccctc  gtattggagc  tgatagaaaa  atggctggaa  420
agacaagtc  ttgggtcaaa  gatgcaaccc  tgcagcatgt  tttaatgagt  gactggctcg  480
tgagctttac  ttctctatat  aatttgcgtg  agacaaaact  ttgccccat  ttctacgttt  540
gtacctatca  gtttactgtc  ctgttccgag  cagcaggatt  agctggaagt  gacttaatca  600
cagctctcat  atctccaaca  actcgagggt  taagagaagc  tatgagaaat  gaaggatttg  660
aattttctct  gcctttaata  aaagaaagtg  gccataagaa  ggagacagca  tctggaacaa  720
gcttgggata  tggggagga

```

```

<210> 444
<211> 738
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(738)
<223> n = A,T,C or G

```

```

<400> 444
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aaagaaacag  atgatgatac  tagggaatgg  aaacaaaatt  ggaacacctg  gttatttggg  180
gatttatatt  gtactctgca  cagttgcctt  tttttttagg  cgtgttccct  ggaaaagagg  240
gacggatgaa  cctggaagta  agtaaaagac  attctagggt  tgtagcatca  aggcagttaa  300
tatccaagca  tcagctttct  ctttatacat  ctacactgca  tggcctgcac  caaataagga  360
actgaaccag  gggatgtttt  ttacctccac  agctgcctcc  ttccatcana  gcaccttgat  420
gaacttaagt  tctagtcaaa  cgtcattggc  atgtttttct  cccagcattt  aattacaaga  480
ctttttttct  ttggatagga  tcagttctta  agagcagccc  cggttaactg  aggaatggga  540
gcggttttga  tganaaaaat  gggtttggtg  ttcaggatct  ccaattataa  atgtagtctc  600
tcagaccac  attccgtaaa  gatgatttcc  caagtaacgg  tatttgacta  agttgctcca  660
gagtgttagg  ggcaaacacc  agttagtaag  ctcttatga  acaaccccca  tataagtagc  720
ttgtccatt  tgcaggca

```

```

<210> 445
<211> 716
<212> DNA
<213> Homo sapiens

```

```

<400> 445
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tcggcccgga  aggctctctc  cttggcaaga  tgggattccg  ggaggcggtg  gcggccggag  180
acgtggattt  gctcaggtg  cggagccgca  gctacaggag  gatgctcgcg  aggaccccca  240
gagctccgcc  cggagggtac  tgtgaggccg  ttaggagctg  gcggtggatg  acttccgcac  300
tcaaacactg  gagccatcac  acggaagcac  gaggagggtg  tctctcggcg  ctactcccg  360
tcgctcaagg  tgtctctcgc  tgcgccctca  ggtgcgggag  gagctcgagg  cccaactaag  420
ctgcttccgg  gagctgctgg  gcaggggccc  cagcgacgcg  gacgggcacc  agcaagtga  480
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gtccaccgcg  tgcctcggag  cctggcgccg  gtccctggaag  gtaccctagc  ggccacacac  600
ctgacagccg  agctgatggc  gcaccccgcc  taccacagtg  tgccctccac  cgcgcgctgc  660
ggtgaaggcc  ccgacgcttt  ctctttgctc  ttgggaagcg  gcttgcattg  agcttg  716

```

```

<210> 446
<211> 641
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(641)
<223> n = A,T,C or G

<400> 446
gtctncaagctc gcgctccggc ctcaggcaca gcatcccccac gggcctccac gccaacctgt 60
ccgagngccg ccccgtaggt ccggcccgcgc atcgctgctc ggcccggaag 120
gctnttctct ttgcaagatg ggattccggg aggcggnggc ggccggagac gtggatttgc 180
ctcaggtgcg gagccgcagc tacaggagga tgctcgcgag gacccccaga gctccgccc 240
gagggtagctg tgaggccgtt aggagctggc gngngatgac ttccgattc aaacactgga 300
gcatcacac ggaagcacga ggagggtatc ctggcagct actccggtc gctcaaggtg 360
tctntcgctc gccctctagg ngcgggagga gctcgaggcc caactaant gcttccggga 420
gctgctgggc agggccccc cgcacgcgga cgggcaccag cacgtgcacg tgctcccagg 480
nggacagacg ccttcgtggg cctgancact tgcggccggn acatgttccc tcaccccgcg 540
gtccggccgc ttggcgcggg tcctggaagg gccacacctc gacagccgaa 600
ctgatggccc accccggcta cccangtgt gcctccacc g 641

<210> 447
<211> 652
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(652)
<223> n = A,T,C or G

<400> 447
gaattcgaa cccctcgctt ttagaaaatt gtatatgcag ctggatgaag gcagcctcac 60
ctttaatgcc aaccagatg agggagtga ctactttatg tccaagggta tcctggatga 120
ttcgccaaag gaaatagcaa agtttatctt ctgtacaaga acactaaatt ggaaaaaact 180
gagaatctat cttgatgaaa ggagagatgt cttgtagtac ctgttaact tgataattt 240
tagaaatcag ttcttgccaa atgcactgag agaattttt cgctcatatc atgcccctga 300
agagcgtgga gagtatcttg aaactcttat aacaaagtcc tcacatagat tctgtgcttg 360
caaccctgat ttaatgcgag aacttggcct tagtcctgat gctgtctatg tactgtgcta 420
ctctttgatt ctactttcca ttgacctcac tagccctcat gtgaagaata aaatgtcaaa 480
aagggaaatt attcgaaata cccgcgcgc tgctcaaaat attagtgaag aattttgtan 540
ggcatcttta tgacaatata tacccttatt gggccatggn ggctggcata aaaaagcacc 600
aattggctaa ggaactttcaa gttttttact ttcaagaactt aaaagcttac cc 652

<210> 448
<211> 677
<212> DNA
<213> Homo sapiens

<400> 448
gaattcgaa cccctcggcg cctggcagag gtgaaggact ccctggacat cgagggtcaag 60
cagaacttca ttgacccctt ccagaacctg tgcgagaaag acctgaagga gatccagcac 120
caactgaaga aactggaggg ccgcgcgcct gactttgact acaagaagaa cgcgcaaggg 180
aagatcccc atgaggagct acgcagggcg ctggagaagt tcgaggagtc caaggagggtg 240
gcagaaacca gcatgcacaa cctcctggag actgacatcg agcaggtgag tcagctctcg 300
gcctgtgtg atgcacagct ggaactaccac cggcaggccg tgcagatcct ggacgagctg 360
cgggagaagc tcaagcgcg gatcggggaa gcttcctcac gccctaagg ggagtataag 420
ccgaagcccc gggagccctt tgaccttgga gagcctgagc ggccttcccc 480
tgaccacag ccccaagat cgcagcttca tctgtcttcc gatcttccga caagcccatc 540
cggacccta cccgagacat gccgccctg gaccagccga gctgcaaggc gctgtacgac 600
ttcgagcccg agaacgcagc ggagctgggc ttcatgaggg cgacgtcatc acgctgacca 660

```

accagatcga tgagaac

677

&lt;210&gt; 449

&lt;211&gt; 603

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(603)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 449

```

ttttttgtan aaagagacat ttaatacttc tgtttacaaa attcaggcgt acatttcagt 60
ttgccctgga ccgtgcccaa agctgtgtgc tcactctctgc gccctcatg tactctctgac 120
gaggggggtg cagggcaggg cagagcagag cctgggggtcc ggaggcttca ctggaccaca 180
ggggggaggg aatgtgaatg tggcctggcc canagaaactc cccatttcat cgatttttga 240
ttgggcgata gaggaagcag atgtcggggc tgccctgcctt ggtctanagg agatggctgg 300
ggccacttcc cacagggtga agtggcagcg gctcagcaag gggagcctgg ccaccagggg 360
ctgggacatg cgctcactgg aacctttgtg cttggccctc ggcagcgcgg ctgtggtccc 420
gtgtgagggtg tgctgggggtg ggggtgtgggt ggctggtggt ggcagcttgt gccagagtga 480
cacaggcctc cctgggttgg gatgggggca agttaaaaag ctgaaaagggt acctggcttt 540
ctgagggcgg gcttggggagc aggcctctgca gganaccatg ttctctgtcc tcagcagatc 600
cac

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603

&lt;210&gt; 450

&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(678)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 450

```

gaattcgac cccttcgcat caatataana tgccaccocat ctgcagttaa ttctttttcc 60
tcactcatgtg attaaaaagtg gtgattcagt gggaactggg aatgttttta gctgggtgga 120
gaaggctgccc tacactgggac actgttttagt attctcatat catttaaaca gcaaggaggt 180
tcagggaaga ataacctgtag ccttgggttaa tccactaggg cttttgtgag taggagagct 240
gatactcac attcttagca ggtgaaaactc tgccatgatg gaaacagata gtgaagagtt 300
actgacgtat cccaaattat atgctgtgac ataaattccc agcatgccca gccctgattt 360
ctgagttcat aagtaattct agtgaacctt agtaggaatt ctgggtaaga aaatgaggtt 420
gccatttgct ttgtttgcat caccagacc agacatccag aagagccctc cacttgaaa 480
agcagacaga ttttaaatta accccctcct tcocactcac cttcatctcc ctaagagttt 540
tgggcattta attccacatt ttgaaaggaa tacattgggtg aaatttggga agagaatctg 600
tgctatgcaa tgtttcatta aaattcttcat tttttcaagt ctctctaaaa ataatttga 660
gatctatctt ggatggat

```

678

&lt;210&gt; 451

&lt;211&gt; 651

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(651)

&lt;223&gt; n = A,T,C or G

```

<400> 451
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aaaccaagat tctgtacaat attctaacaat tatattgtaca taaaattata ttactcataa 120
ctatatgtgaa aagtcattatt tgtagaatat ggctggcaac aaagaaagac ccataccatt 180
tagcgttttga agcaggggcag gtagcaagag aacattagca aagacacctt tgtgcctgga 240
tacacaatcc tgcctactaag ttatgtgact aaccagcaca ctctaagttc tgtggtttgt 300
tcgttgtttc acattcttagt agggaaattct gcagcaggcg atgcgaaaaa naaacattgg 360
tcaaatgaaa tgtgaaatgc tgtttaaaaa ctgcataatt gctatgataa tgggtttgng 420
aatccaagtt gcattggaag ttcaactcatt ctccattcat tatgcattgcc tccagtgatt 480
taatgaattt cagcaggngg aaaaagacagc ttgaaacaga tcagatgggc tgtgagtcn 540
attcttgatt ctttttcctc attttggctcc tgaatgtttgc anaaactcgg tttgtacac 600
tggggaagga gagagtgaag accctccagt tggttcctca gtcagctccg t 651

<210> 452
<211> 679
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(679)
<223> n = A,T,C or G

<400> 452
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aagcctggcc agacctggaa gaacaaagag catcatctct ctgacagaga gttttgtgtc 120
aaagaacctc agcaggtagt acgtagagct cctgagccac gagtgtttga cagagagggt 180
tgtgtatgaa tcagcctgtc acccacaggt gtatctaggg tctgtttgta tccctggcttt 240
gttgacgtga aagaagctga ctggatattg gaacagcttt gtcaagatgt tccctggaaa 300
cagagggacc gcatacagaga ggatataact tatcagcaac caagacttac agcatggtat 360
ggagaacctc cttacactta ttcaagaatc actatggaac caaatcctca ctggccaccct 420
gtgctgcgca cactaaagaa ccgcattgaa gagaacactg gccacacctt caactcctta 480
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tcactaggga ggtgccccat tattgcttca ctaagttttg gtgccacagc cacatttgag 600
atgagaaaag agccaccacc agaagagaat ggagactaca catatgtgga aagagtgaag 660
atacccttgg atcatgtgta                                     679

<210> 453
<211> 630
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(630)
<223> n = A,T,C or G

<400> 453
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tgccattgga caggacatcc agccccaaaag agacctcacc cgctttgtga aatggccccc 180
ctatatcagg ttgcagcgcc agagagccat cctctataag cggctgaaag tgccctcctg 240
gattaaacag ttaccccagg ccctggaccg ccaaacagct actcagctgc taaagctggc 300
ccacaagtat agaccagaga caaagcaaga gaagaagcag agactgttgg cccgggccga 360
gaagaaggct gctggcgaag gggagctccc aacgaagaga ccacctgtcc ttgcagcagg 420
agttaacacc cgtcacacc ttggttgaga acaagaaagg tcagctgggt gtgattgcag 480
acgacgtgga tcccatcgag ctggtgtgtct tcttgctctc cctgtgtcgt aaaatggggg 540

```

```
tccttactg cattatcaag ggaaaggcaa gactgggacg tctagtccac aggaagacct 600
gcaccactgt cgccttccac aggtgaactc 630
```

```
<210> 454
<211> 677
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(677)
<223> n = A,T,C or G
```

```
<400> 454
gaattcgaa cccctcgccc gcatcgcgna catccccctt gccccagggt cagactggcg 60
cgatctgccc aacatcgagg tgcggctctc agacggcacc atggccagga agctgcggta 120
taccacacat gacaggaaga acggccgcag cagctctggg gccctccgtg gggctctgctc 180
ctgctgtgaa gccggcaaa cctgcgaccc cgcagccagg cagttcaaca cctcatcccc 240
ctggtgcctg ccccacaccg ggaaccggca caaccactgg gctggcctct atggaaggct 300
cgagtgggac ggctcttcca gcacaaccgt caccaacccc gagcccatgg gcaagcaggg 360
ccgctgtctc caccagagc agcaccgtgt ggtgagcgt cgggagtggt cccgctccca 420
gggcttccct gacacctacc ggctcttcgg caacatcctg gacaagcacc ggcagggtggg 480
caatgccgtg ccaccgcgcc tggcaaaagg attggcttgg agatcaagct ttgtattgtt 540
ggccaaagcc cgagagagtg cctcagctaa aataaaggag gaggaaagct ctaaggacta 600
gttctgcctt ccgtcacccc ctgtttcttg caccaggaat ccccacaat gcacttgatg 660
gtggggtttt aacatgt 677
```

```
<210> 455
<211> 598
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(598)
<223> n = A,T,C or G
```

```
<400> 455
ttttttggtt tataggagag atttatttga agaaatatta caacatataa aaactacata 60
aagctcttaat ttccactcat acagtggtag atttgatata atgcataata aaaaactttt 120
aaaattccaga atgcacaaag tactgcacaa ttgatcaact aaatcaattag ttgataagcg 180
aacctcacac aacagcttca tgtcagccaa ggccacaaac accatgtacc acacatgtga 240
acggacagat tgacatgtta aaaacacaac atcagtgcac gttggggatt cctggtgcc 300
gaaacagggg tgacggggagg gcagaactag tccttagcag ctctctctct ctttatttta 360
gctgaggcac tctctcgggc ttggcccaac atacaaagct tgatctccaa gccaatggct 420
ttggccaggg cgggtggcac ggcattgccc acctgccggt gcttngtcca ggatgttgcc 480
cgaagagccg gtatgtgtgc aagggaagcc cctggggaag cgggcacact cccggacgct 540
naccacacgg tgctgntttt ggggtggagca ccgcgccctt gcttgcccat gggctcgg 598
```

```
<210> 456
<211> 574
<212> DNA
<213> Homo sapiens
```

```
<400> 456
ggaattcgaa ccccttcggg gcggggagcc ccgtagaacc gagggggctg gccccgggggt 60
ccgggggag gtggagatgg tgaaggggca gccgttcgac gtggggccgc gctcacagca 120
gttgcatgac atcgcgagg gcgcgtacgg catggtcagc tcggcctatg accacgtgcg 180
```

```

caagactcgc gtggccatca agaagatcag ccccttcgaa catcagacct actgccagcg 240
cacgctccgg gagatccaga tctctgctcg cttccgccat gagaatgtca tcggcatccg 300
agacattctg cggcggtcga cctcggaagc catgagagat gtctacattg tgcaggacct 360
gatggagact gacctgtaca agttgctgaa aagccagcag ctgagcaatg accatatctg 420
ctacttcctc taccagatcc tgcggggcct caagtacatc cactccgccca acgtgctcca 480
ccgagatcta aagcctcca acctgcttca tcaacaccac ctggcgacct ttaaaatttg 540
tgaatttccg gcttggtccc cggattgtccc gaat 574

```

```

<210> 457
<211> 546
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(546)
<223> n = A,T,C or G

```

```

<400> 457
ttttttgaca catctctata tttatatatt agacgggtca gggagggtggc agggggcgccg 60
ggctctccac gcccccacgc tccactcttg ctcaccacac acagaagcag cgagggcagc 120
cgaagtgaca gctttgacag ggaggggatt cggcccggcc tggctcctca gggatgctat 180
cccttgagac taaggaattgt tccttcaggg aaactagggt ggggtttgaa tganatgagg 240
ggggcaggca tggccctgag tcctactca gcgccccca cctccacct gtcctcttca 300
gcaggttggg gcagccagaa ccttccatt ccagaactgc cagagactgc gacgtgggg 360
aaggtaaggg cgcagcagca gcagcggagg attgaactgg gggcacctga gctcccgagg 420
ccccgtgggg agggcggtg gggaggaaaa ggccttgccc tgcctgaagc tggaggcctc 480
agcaaggag agaggtggcc agggccatgc tccaccocgg ctgggctgc caanggtccc 540
gggctg 574

```

```

<210> 458
<211> 674
<212> DNA
<213> Homo sapiens

```

```

<400> 458
gaattcgaac cccctcggtt ttattaagaa ctaagagaat agcttggccg atacaaatgg 60
aaacaccttc caaatgagtc ggagaaaatg tcttgagta ttatgggtaa aatagcaaa 120
agcttgggaa tacagtttgc taatatcaag tccttaacaa cgaccattct tcattcaaga 180
ttagttgtgt ataaatcatc gcttcttcag gagttgactt agaaaaacaag caaacaaaca 240
aacatcagaa actatttaca actgggagca atccttgaag aacataaaga atataaatat 300
caacaaagc tgaaaactct tttttagatt aaagatcaaa tggacatgtc atcggaaatg 360
attgtatggc tcttgattaa atcctggagc aaagtggaga gtgaggaaca actgtaaaga 420
atgtgaatc ggactgtgta ttatagaaca gtaccataaa tttcctggat gggataatta 480
tgtttgact atgtaagaga atattttgcc cttagaagat atatgatgaa gcatttagaa 540
gtaaaatgat atgacatctt gcaaaataact ttcaagtgat tcagccagat atataaaaat 600
tatataaac acattatata atttatatat atataaattat aatacattat ataatttata 660
cattataatt atat 674

```

```

<210> 459
<211> 682
<212> DNA
<213> Homo sapiens

```

```

<400> 459
tttttttaaa tccattggctt gttaattgtc atcccagtta ttacatgtg actatagaga 60
ctgcattctc ccagctgcga gcccgccagg gctttgccac tggatataatt tataacacga 120
ctaattaaaa tgaatttgct tgcaataagg ttctgtgtgc tatittgtgg agaggagtta 180

```



```

ttaaaatttt  cagtacagta  atagtaaact  tgaatgcaaa  gtaataataa  tcatacattt  240
ttaatttcat  gtttaatacc  catttggcta  atgtagaact  attctgaaaa  ttacttggga  300
tcagcacaaat  gtccttttgt  gcttagtagt  atccaaagac  atcctcttga  atgggcttag  360
caatatgcac  tgtcatcaag  atacagctgt  ttgatgcagc  acacacagtg  tgttcctatg  420
atactttgca  caagatcagc  tatgacaaat  acaagttcat  tttgcttatt  gcaggcaaat  480
aatgtccctt  gcaggaaact  ggaaggagcc  agaggccatt  attctaagtg  aaatacctca  540
ggagtggaaa  accaaatacc  atatgttctc  acttacaagt  gggaactaag  ctatgggtac  600
acaaacgcat  atagagtggc  ggaactctgc  gactcatact  acataattgag  tacaatgtac  660
actacttggg  tgatgggtgc  ac

```

```

<210> 460
<211> 663
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(663)
<223> n = A,T,C or G

```

```

<400> 460
gaattcgaaac  cccttcgcgg  ggcgcgcgag  cggcgccagc  tcgggggcagc  ggaaccacaga  60
gaagctgagg  gggcggttagc  ggcgcgcgag  gcgacgcaga  cgactcccg  cgtgtgccc  120
agcctcttcc  cgccgcagcc  gcccttttcc  tcctccctt  acgtcccca  gtgcggcagt  180
accgcctcct  tcccagccgc  gcggcttctc  ccagacctct  cgccgcgggt  gagccctatt  240
cccagaggca  ggtggtgctg  accctgtaac  ccaaaggagg  aaacagctgg  ctaagctcat  300
cattgttact  ggtggggcac  atgtccttga  agcttcaggc  aagcaatgta  accaacaaga  360
atgaccccaa  gtccatcaac  tctcgagtct  tcattggaaa  cctcaacaca  gctctggtga  420
agaatcaga  tgtggagacc  atcttctcta  agtatggccg  tgtggccgcg  tgttctgtgc  480
acaagggtca  tgcttttgtt  cagtactcca  atgagcgcca  tgcccgggca  cgtgtgctgg  540
gagagaatgg  gcgggtgctg  gccgggcaga  ccttgacat  caacatggct  ggagagccta  600
agcctgacag  acccaagggg  ctaaaganaa  gcagcatctg  gcatatacac  gctcttcgac  660
tac

```

```

<210> 461
<211> 612
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(612)
<223> n = A,T,C or G

```

```

<400> 461
ttttttggga  tccaatctnt  ttattgtcag  ggtcccttcc  ctgnggcccc  ccgccaacac  60
tatagaaaaa  accaaagcct  gggagtgtcc  tggggagggg  aggtagtatg  gggaaacccc  120
tgtgtcttac  cctntggcct  gggcagtgca  nacaggagg  gctcatgggg  aaggagttag  180
ccagtaactc  cactgcana  ggacatggca  ctggctggga  tgcgttgggg  gaggaggcgc  240
ctgctgcag  ctttctntg  gtaccgcctg  gggggtggca  tccagggttg  ggtgcccgcc  300
ttgaggcctg  gggcagcgat  gcccttcacc  tgctggnggc  cattgctcct  gtcaggctgc  360
ttactgcaag  gccccatcat  ccgcgtctgt  gtcttgctgt  tgttccagct  ctctctcgct  420
gngtgtcagg  agcccttctc  catcgccgtc  gtctcggttc  cgtgcttccc  cctggggcag  480
gctgctccta  naagttgtgt  tctcttgggg  ggctggtggt  cggttgttgc  caccgcacc  540
caccaccact  ggcaccggca  ccgntgcacc  accaccgcgc  ccgcgcgcgn  tggngccacc  600
ttcatcacc  tt

```

```

<210> 462

```

<211> 672  
 <212> DNA  
 <213> Homo sapiens

<400> 462  
 gaattcgaac cecttcgggat ggaagggggc ggggcagcgt cggggaaaag aagggccgga 60  
 ggcgcggcgg cgggcggcgg agagggggcg cggcgcgggc ggcggcgggg ttcccgcgcc 120  
 gcggagcccg gcccgagagc cgcgtccacg ttctctgcctc ctgctcccg cgccttgggg 180  
 cgccgccatg acgcccgatc tgctcaactt cagccccaga tgtcaccaag ctctcggaact 240  
 ctaacaagga gaacgcgctg cacagctaca gcaccagaa gggccccctg aaggcagggg 300  
 agcagcggcg gggctctgag gtcactcagc ggggtggccc tcggaaggcg gacgggcagc 360  
 gtcaggcctt ggaactacgt gagctctcgc cgctgaccca ggtctcccg cagcggggccc 420  
 gcaccccagc ccgcactcct gaccgccctg gccaaagcagg agggagctgga gcgggacctg 480  
 gccagcgctg ccgaggagcg gcgcaagtgg tttagggcca cagacagcag gacccagag 540  
 gtgcctgctg gtgagggggc gcgcggggcg ctgggtgccc cctgactgag gaccagcaaa 600  
 accggcttag tgaggagatc gagaagaagt ggcaggagct ggagaagctt gcccttgcgg 660  
 gagaataacc gg 672

<210> 463  
 <211> 562  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1) ... (562)  
 <223> n = A, T, C or G

<400> 463  
 tttttaaag tataaagtgt ttggaaaaa aaggaaaaan ntctatataa aaatctcttc 60  
 acatataaaa tcttgaagaa ggtgcaaggt gagaccagat gcgagggcg tgctcagata 120  
 tgacgtgtgt gtgtgtgtgt gtgtgtgtgt gtatccgtgt gtacatgtgt gcaagtgtgt 180  
 cggtatgtgt ctgtgtgtct gtgtgtgtgt gtgtgtgtgt ggtgggtgca 240  
 agtgcacgtg tggcccacag aggggtggga gaaagcttgg ctttttactt ccatccagga 300  
 ggaaaggagg gcggctggtc ctccagcctg gagggtctgc agctggggcg gactctact 360  
 cagccaggct gttgcgcacg gactccttct cctggaggcg ggcattggca agacgcaggt 420  
 gctccttcag ctgctcgatc tcccgctcag accgtgtctt gatgtggctc aactccacat 480  
 agacgtcctg gtactttccc naggtgaagc gcttgtcctt ctgcatcatc tggagctcgt 540  
 ccgcaggga ctgcaccttc ct 562

<210> 464  
 <211> 553  
 <212> DNA  
 <213> Homo sapiens

<400> 464  
 gaattcgaac cecttcggga ccaggaaccc agggagagcat ggccacgctg cgccggcttc 60  
 gggaggcgcc gcggcactta ctgggttgcg agaaatccaa cttcggaac cacaagtgcg 120  
 gccaccggca tcttctgcag acgcactact ataactacag ggtttcattt ctacttccgt 180  
 aatgtgggat actatcggaa gaactgaaaa acctggctcat gaacactgga cctatttact 240  
 ttgtgaagaa ttactcttca catgaattaa ttacactgta attcatcagt acctttataa 300  
 agaaaaggttc ttgctatgca ctaacatata atacacatat tgatgaagat aataactgtt 360  
 ccctgctacc aaatgggaaa ttaattttgt cactggataa gaagaaactg 420  
 gacttcaggg tcatccatct cagttttctg gcagaaaaat tatgaaattt agtcagaaag 480  
 aatcgacaaat gatgtcatat ttttccaagt accaaattca ggagcatcag ccaaaagtag 540  
 cactgagccc gtt 553

<210> 465

<211> 383  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(383)  
 <223> n = A,T,C or G

<400> 465  
 tttttggaag aaaaacacgat ttttaatttt tatttttttat gggggacagn gatcatttgc 60  
 cccaacagcc atntgaagcc aatagtctctg attattaaaa atcacaaaagt tatataaatg 120  
 ntctctctct tttcgaaaac catgttcatt tttttcccaa naaacagggc tgctctgcaa 180  
 gccttgaaac gacagngtaa cccatggagc taacttcggt tcatcaaaagt agngacagan 240  
 atgttccaat agganacaga tcttntntgg aagtataag ccagngattg tacacaataa 300  
 agcttttgcc accactgtgc ttggctcagg acagcaatag gttgatatga aattattagg 360  
 ctcatatttt agnncgacat tac 383

<210> 466  
 <211> 673  
 <212> DNA  
 <213> Homo sapiens

<400> 466  
 gaattcgaac cccttcgctc cctcctgcac gcaatggtgg cctatgatcc cgatgagaga 60  
 atcgccgcccc accaggccct gcagcacccc tacttccaag aacagaggaa aacagaggaa 120  
 cgggctctgg gcagccacag aaaaagctggc ttcccgagc accctgtggc accggaacca 180  
 ctcagtaca gctgcacagat ttccaaggag ggcagaaaagc agaaaacagtc cctaaagcaa 240  
 gaggaggacc gtccaagag acgaggaccg gcctatgtca tggaaactgcc caaactaaag 300  
 ctttcgggag tggctcagact gtctgtcttac tccagcccca cgctgcagtc cgtgcttgga 360  
 tctggaacaa atggaagagt gccggtgctg agacccttga agtgcattccc tgcgagcaag 420  
 aaggtagcgc ggaaccagct tctctgacgg cgctgctctt cgacccagcc caggccgcca 480  
 ctgaattttt tgtctgtaat ttttctttga cagacagatc cgcagaaagga ccttaagcct 540  
 gccccgcagc agtgtgcctt gccaccata gtgcggaaag gcggaagata actgagcagc 600  
 accgtctctc gcacttcgga ggcaacacca agcccagacc ggccaggcct ggggtgatctg 660  
 ctgctgagac gcc 673

<210> 467  
 <211> 373  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(373)  
 <223> n = A,T,C or G

<400> 467  
 tttttactgg aacgacagct tatnttttaa taaaagtcag gggngtcagc agngtcactg 60  
 gtaanacatg atggcgctcc acgactgacc agcagcgctg ggaaggagaca cgcanaaccc 120  
 accttccaac cagccccaac acatnacana aatgcctgct cgtttgtttt gattcatata 180  
 caaagttaca aagtatttcc tgcccacaat nttaacgaa aatgaaagaa aaccttanaa 240  
 tgcggggggt ttacaagtat attagcccan aacatcctag gcagctgcnc gggccgcggy 300  
 tgcggcaggg cgccggggcaa caccacaaagc ccgycgcagc gcgaaaecga cgcaggcgca 360  
 tcccagccc tcc 373

<210> 468  
 <211> 573

<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(573)  
<223> n = A,T,C or G

```
<400> 468
gaattcgaac cctctcgctg ctgtcctact tgatgcttgt cactgtcatg atgtggcccc 60
tngctgtgta ccaccgactg tgggatacgag catatgtgag gctgaagcca gctctgcagc 120
ggctagactt cagtgtccgt ggctacatga tgtccaagca gagagagaga caattacgcc 180
gcagagctct ccaccagaaa cgagccatgg acaaccacag tgacagcgaa gaggagcttg 240
ctgcctcttg tctcagctg gacgattcta ctgttgccag ggaattggcc atcacagact 300
ctgagcactc agacgctgaa gtctcctgta cagacaatgg cacattcaat ctttcaaggg 360
gccaaacacc tctaaccgaa ggctctgaag acctagatgg tcacagtgat ccagaggaat 420
cctttgccag agacctcca gacttccctt ccattaatat ggatcctgct ggccctggatg 480
atgangacga cactagcatt ggcatacgcca gcttgatgta ccgttctccg ccaggggggct 540
gaggaggcccc aaggccccac ctgccagccc ggg                                     573
```

<210> 469  
<211> 635  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(635)  
<223> n = A,T,C or G

```
<400> 469
tcnccatcta gaactagggt ggacaggctt gctcaagttt caccagagtt antactggcc 60
tctgttcgca gaggtttttag ttnnacactg cagaattggc agactacacg gtttatggaa 120
gttgaaagtag caataagatt gctgtatatg ttggcagaag ctcttccagt atctcatggg 180
gtccacttct cagggtgatgt ttcaaaaagct agtgctttgc agggatatgat gcgaactgta 240
agtatactgg agataatttt gaccataaat ttctgttttc agtataagct aatgggagtt 300
ccttaattgt tagagcttag tatatgttaa taccggggca ttttgatgtt gcaataaata 360
agaagaggtt tcttaacttt ttctgatctc agctggtaac atcaggagtc agttcctatc 420
agcatcacatc tgtgacattg gaggttcttc aaactggtgt tagatatgaa aagtttttca 480
cagttgaacc tcagcacatt ccatgtgtac taatggcttt cttagatcac agagggtctgc 540
ggcattccag ngcaaaagtt cggagcagga cggttacct gttttctaga tttgtcaaat 600
ctctcaataa gcaaatgaat cctttccttg aggat                                     635
```

<210> 470  
<211> 593  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(593)  
<223> n = A,T,C or G

```
<400> 470
gaattcgaac ccttcgggtat taacaaatat ntacatttct atttttataa tcataaagga 60
tatgcctggt ttaaataaca tacatatata caatatctat caggaaaacc ctcaagacag 120
ctctcagtta aaaccttngn tgctgtcttc tcaaaatata ttataaaaaa tttgtcaggg 180
ccaaatccat acttcagaaa taattcatca aattttatatt ttaagnaaaa agtaaccttt 240
```

```

caggcatttc agcagcatatc attgacaatc taggggtatat atgtatgtat gtttcttatt 300
gtatgtctat atatgtatgt ggggaggaca ggagtgaatg ttcacacact tttcttgcgt 360
actcaactaa attggagaat gtttctgaag aaaattggat gaattagct gctgagattg 420
agtttctgcc ttaaaatctg aaacaaaaaa agggacaaat tgctggtang atctactgac 480
tgtngccatc accagaacac tttagtttctt cccagacatg aatttctctga caggctctga 540
gccagaataca cactgtgggc gtgcantnrg gtcacccctg atatgcctcc act 593

```

```

<210> 471
<211> 581
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (1)...(581)
<223> n = A,T,C or G

```

```

<400> 471
tttttttaac cangggacat ttattaacat gcttcaaaag tgaccaaaagt gtcacgccag 60
cacaatagcc gaggcaatca acgttctctt agtgtgtgat ctgctccaaa acaccaata 120
aatagggtta ggaataacct caaataaatt gtaatttaac ttcgccccaa attatacatc 180
ctctactgct ctccctgct cctgtaaaga tactagcggg aggggagaaa gctcaaatga 240
ctctgtaatt tagaattaca accagagaag aaatacttca agcacataaa agacgttcca 300
ttgaagagcg acattcattc tgggaatgtt gttttgaaaa caactcttnt gggggaatc 360
aaaaggctac gaacaaagca acataaagta agttttgggt tgttttgcaa aataaaaaata 420
tacaattgag tggaccagat ggcaaaaaaaca taccaattac aatctgaatg ctatatattaa 480
aacccttaaa ttctgaaggc ctgaatatca acaaacctat ttatgtttat gatcctaaaa 540
agacattaaa tattattaaa ccccaactt ccaaaacata g 581

```

```

<210> 472
<211> 674
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (1)...(674)
<223> n = A,T,C or G

```

```

<400> 472
gaattcgaac cccttcggat ggcgatgatg ntcacagaaa gttctccgct cccagacatg 60
ggtccctcgg ctctctgctt cggaaagcgca gcagcaggca tctgtgggaag gtgaagagct 120
tccttaagga tgaccctgcc aagcccggtcc acctcacagc ctctctggga tacaaggctg 180
gcatgactca catcgtcggg gaagtgcaca ggccgggata caaggtgaac aagaaggagg 240
tggtggaggg tgtgaccatt gttagagacac caccatgggt ggttgtgggc attgtgggct 300
acgtggaaac ccctcgaggg ctccgggacct tcaagactgt ctttgcgag cacatcagtg 360
atgaatgcaa gaggcgtttc tataagaatt ggcataaate taagaagaag ccctttacca 420
agtactgcaa gaaatggcag gatgaggatg gcaagaagca gctggagaag gacttcagca 480
gcatgaagaa gtactgccaa gtcatccgtg tcattgccca caccagatg cgctgctctc 540
ctctgcggca gaagaagccc acctgatgga gatccagggt aacggagcca ctgtggccga 600
gaagctggac tgggcccgcg gagangcttg agcacaggta cctgtgaacc aagtgtttgg 660
gcaggatgaa aatg

```

```

<210> 473
<211> 646
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(646)
<223> n = A,T,C or G

<400> 473
ttttttcagn gaaaaataac ttttattgan accccaccaa ctgcaaaatc tgttctctgc 60
attaagctcc tnttctcttt gcaattcggg ctttcttcag nggtcccatg aatgctttct 120
tctctctcat ggtctggaag cggccatggc caaacttgga gngngtgta atgaacttaa 180
ggtcaatctt ctccanagcc cgccognttc tctgcaccag caaggacttg cggagggtga 240
gcaccogctt ctgtgttccc accacacagc ctttcagcat gacaaaagta ttggtcactt 300
caccatagng gacaaaagcca cccanagggt tgatgctctt gtcanatagg tcatagtcag 360
tggaggcatt gttcttgatc agcttgccgt ccttgataag gttagccctg ccaatcttat 420
aaatcttctt gttgatctca gtgcggtgat ggtagccctt ctgcccacgc cgtgccacag 480
agaaggctac acgagcagga tgccatgccc caatacaggc caccttgcgc aggctcgtg 540
gggtcttgcc gggcagcttc ttggtgtgcc aacgactggt gaccccttg tagcctttgc 600
ccttggtcac ccgatgacg tcgatcatct catcctgccc aaacac 646

<210> 474
<211> 544
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(544)
<223> n = A,T,C or G

<400> 474
gaattcgaac cccttcggca gcacactccc antggccgc agcctgacac gccgcgcggc 60
ccccagctct ccgcggctg ctccccacag catggcacag ggcctcgcc cactatggca 120
gcagcacggc acagcacgct cgaactcatg ctgcggccca aagctgatgg tgagacactt 180
ctaaaaggcc tccagtcact ttccaggag caggggatgg cggagctcgt gcacacctgg 240
caggaccatg gctatttagc aacctacaca aacaagaacg gcagctttgc caatttgaga 300
atttaccac atggattggt gttgctggac cttcagagtt atgatggta tgcgcaaggc 360
aaagaagaga tcgacagtat ttgaaacaaa gttagagaaa gaatgaaaga attgagtcag 420
gacaagtact gggcgggtga aacgattacc accatagtg cgaggaggag ccatcgacag 480
atactggccc accgncgacg ggcgccttgg ttgaatatga catagaatga agtgggtat 540
gacg 544

<210> 475
<211> 578
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(578)
<223> n = A,T,C or G

<400> 475
gaattcgaac cccttcggga gaaccccatg ngggaacttc gcatccgcaa actctgtctc 60
aacatctgtg ttggggagag ttgagacaga ctgacgcgag cagccaaggt gttggagcag 120
ctcacaggcc agaccctgt gttttccaaa gctagatata ctgtcagatc ctttggcatc 180
cggagaaatg aaaagattgc tgtccactgc gggccaaaggc agaagaaatc 240
ttggagaagg gtctaaaggt gcgggagbat gagttaagaa aaaaacaact ctcagatatt 300
ggaacttttg gttttgggat ccagggaacac atcgatctgg gtatcaataa tgacccaagc 360
attggtatct acggcctgga cttctatgtg gtgctgggta ggccagggtt cagcatcgca 420

```

```

gacaagaagc gcaggacagg ctgcattggg gccaaacaca gaatcagcaa agaggaggcc 480
atgcgctggt tcacgacagaa gtatgatggg atcatccttc ctggcaataa aattcccggt 540
tctatccaaa agagcaataa aaagttttca gtgaaaaa 578

```

```

<210> 476
<211> 619
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(619)
<223> n = A,T,C or G

```

```

<400> 476
ggaattcgaa cccttcgct cctgcctgct cgccatgttt tcaggncggg nctggcttgg 60
tcttccccgc taaggaaatg gccggggagc tcagggggac ccaggcgccg tcgcttcggc 120
ggagcctggg ctgaccagcc aggcagcggg ggtaaaccgc acaattctg cgcgaggtag 180
ggaggccatg gcgtccggca gtaactggct ctccgggggtg aatgtcgtgc tggatgatgc 240
ctacgggagc ctggtgtttg tactgctatt tatttttggg aagaggcaaa tcatgcgctt 300
tgcaatgaaa tctcgaaggg gacctcatgt cctgtgggga cacaatgcc ccaaggactt 360
gaaagaggag attgatattc gactctccag ggttcaggat atcaagtatg agccccagct 420
ccttcagat gatgatgcta gactactaca actggaaacc cagggaaatc aaagtgtgta 480
caactatctg tataggatga aagctctgga tgccattcgt acctctgaga tccatttca 540
ttctgaaggc cggcatcccc gttccttaat gggaagaat tttccgcttc taccttgctg 600
gatcttgcga aacactagt 619

```

```

<210> 477
<211> 674
<212> DNA
<213> Homo sapiens

```

```

<400> 477
gaattcgaa cccttcgggg tggtcgactg ctagagccga gcgaagcgat gcctaaatca 60
aaggaacttg tttcttcaag ctcttctggc agtgattctg acagtggagt tgacaaaaag 120
ttaaagagga aaaagcaagt tgctccagaa aaacctgtaa agaaaacaaa gacaggtgag 180
acttcgagag ccctgcctatc ttctaaacag agcagcagca gcagagatga taacatgttt 240
cagattggga aaatgaggtg cgttagtggt cgcgatttta aaggcaaatg gctaatgat 300
attagagaat attgatgga tcttgaaggt gaaatgaaac caggaaagaa aggtatttct 360
ttaaattcag aacaatggag ccagctgaag gaacagattt ctgacattga tgatgcagta 420
agaaaactgt aaaattcgag ccatataaat aaaacctgtg ctgttctagt tgttttaata 480
tgtcttttta cactggcctt tgttttctaa atgttctcca agctattgta tgtttggatt 540
gcagaagaat ttgtaagatg aatacttttt tttaatgtgc attattaaaa atattgagtg 600
aagctaattg tcaactttat taaggattac ttgtctcgcc cacccttagt gtaaaaaaaa 660
atcaagtaat acat 674

```

```

<210> 478
<211> 663
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(663)
<223> n = A,T,C or G

```

```

<400> 478
tttttttaag ctttcacaat ttttattaaa tctagtcta nttagaacaat atctgatgtt 60

```

```

acagacatca tccccggtg aacatgttta ataagtgaag gcaagtcaga catctcatct 120
aagtcattat ttctgcgaga ctaagcaata actacacaga acacatggg taaacaaca 180
cctgctcagt ttccacacaa gccatgttgt ttatcaaat agatctgcta atattgaata 240
cagtagattc ggtgattgta gttctcatat aagtatctta ttgagataac attttgacag 300
tttctactgac ttccaaata agcataccat aatcaaagaa aagaataaag agtgaagtaa 360
aaactgaaca tgaagagatt aagttattaa aggaaaatga agtaataaaa aagagtgaag 420
aacccattggg ggtggaagtc aaacaagcct agacatttga ttggaagaga aaagatcaaa 480
tatgaagttc acaaaccaaa agttttataa ctcaatgcaa tacaatcct ttttattgta 540
aaagctgagt tgaactaaa agatctataa aaactgttac ttttgcctt aaacagtacc 600
aactcttatg atcaaaaaag gccacacagt taagattgna ttacttgatt ttattttaca 660
cta 663

```

&lt;210&gt; 479

&lt;211&gt; 673

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 479

```

gaattcgaac cccttcgaat gaagaactct ccagggatct agtgaataaa ctaaaaccct 60
acatgagctt cctgactcag tgccgtcccc tgtcagcgag catgcacaac gccatcaagt 120
tccttaacaa ggaaatcacc agtgtgggca gttccaagcg ggaagaggag gccaaagtcag 180
aacttcgagc agccattgat cggtagtgac aagagaagat tgtgctagca gctcaggcaa 240
tttcacgctt tgcttaccag aagatcagta atggagatgt gatcctggta tatggatgct 300
catctctggt atcacgaatt cttcaggagg ctgggacaga gggccggcgg tttcgggtgg 360
tagtggtgga cagccggcca tggtctggaag gaaggcacac actactgtct ctagtccatg 420
ctggtgtccc agcctccctac ctgctgattc ctgcagcttc ctatgtgctc ccagagggtt 480
ccaaagtgct attgggagct catgcactct tggccaacgg gtctgtgatg tcacgggtgag 540
ggacagcaca gttagccctg tgggctcgag ccataatgt accagtgctg gtttctgtg 600
aaccatacaa gttctgtgag cgtgtgcaga ctgatgcctt ttgtctctaa tgagctagat 660
gaccctgatg atc 673

```

&lt;210&gt; 480

&lt;211&gt; 203

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(203)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 480

```

gaattcgaac cccttcgggg ggaggaagag gaggtggagg agggagggtga tgttgatagt 60
gatgaagaag aggangaaag tngangananc tcctcggagg gcttggaagg tgaggactgg 120
gccacgggag tagtggaggc cngtggcagc ttcggggcct atgggtgccca ggaggaagcc 180
cantgcccta ctctgcattt cct 203

```

&lt;210&gt; 481

&lt;211&gt; 482

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 481

```

ccagacgctg cccatggagg cgtccagcga gccgcgctg gatgctaagt ccgatgtcac 60
caaccagctt gtagattttc agtggaaact gggtagtgct gtgagctcag acactgtcac 120
atctcttaag tatccttacg ttgcagtgat gctaaaagtg gcagatcatt caggccaagt 180
aaagaccagg tgctttgaaa tgacgattcc acagtttcag aatttctaca gacagttcaa 240
ggaatttgct gcagttattg aaacggtgtg aagcgggat ctttggttga taaattgcta 300

```



```

tcattctaaa gtcattggact tcacttttcg caacaaaact aaataaggat ggaacattta 360
ttgaatgaaa aatgcacttt tgtttttcca tttttttaa taataaaaat cagacaaaaa 420
gaaaaaaaaa aaaaaaaggg cgccgcctcg agtctagagg gcccggttaa acccgctgat 480
ca 482

```

&lt;210&gt; 482

&lt;211&gt; 505

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 482

```

aaaaatttta gctgccaaga aagaagttta gactctcagt gctgagagag actgaatcca 60
cctagggtgat aagggtgactg gacccagtaa accctttgtg tgctgggggg ttttatgcct 120
tgtagaaccc agtgtgagca agatttgggt accctacata cattcagtag ccaggaaaagg 180
gtgatttgat tgccagactc tgccctgctgg caaaaggatg agctgtagaa gctgaagtcc 240
taggttagtag atataaaagaa gacaaattag gtggcacctt ctgactctgt caatgcattgg 300
atttggaaatt gaatttttcc tctaattatt ctagggaaac cctgggctaa gaaaccaatg 360
taaaaacctga tgaggtagtc tgtagtacac ctgggtagag gttagaggcaa ccacaaaatt 420
attcttaaga atgcctccca ggccgctgga agatgaaact ttctgttgaa tatgagctca 480
tggtaaaaat ttaggctgga tgcag 505

```

&lt;210&gt; 483

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 483

```

tgcaaaaagg taacaaattc ataactggaa agcaaaagaga agaacaagta tgatttggat 60
gataaagcat tgtttttaatg gtgaaaaactt cacagatcac taatgtttct agagggtaac 120
ttcaagtggg caagctgggg tttttaggta gtcagtggcc tagttcctaa agccacagta 180
taggatctgt taaactgaat gtctgttgaa agtttgtttt agctgcttgg aggcctcctt 240
ttaagacaaa ctgtatgtga ttaagttggt ttgagggaaac tgaagaacct gatgtagccc 300
ctggccagat aactgcctga tttctcagat attatttctc tgggaaacat catcatagc 360
acaggagcct aagagtggca ttatctcttc gccttaattt ccagagatta tttctgtact 420
gagaatcctg gaactactat gctaggaaat ttaaagctgc atggctctgc ttgttttcat 480
ttaattattg tgaataccta g 501

```

&lt;210&gt; 484

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 484

```

gcactaagac caccctctat gaggagcagg gtgactacta cagccagtag atccggggcct 60
gcctgggacca cctggccccc gactccaaga gtctctggga ggggaagaa gacgctcttc 120
ttcattacac tgctgctcag ctctcggaag aggggtgtctt ggtggaaatt gaagatcttc 180
cgccctctca cttcagaacac gtcacttttg acatcacgcc ggagatgag gcaggaaagt 240
tgaagtaaa tgccaagttc ctgggtgtgg acatggagcg atttcaagct cactatcagg 300
atctcctgca gctccagtat gaggggtgtgg ctgtcatgaa actcttcaac agggccaaag 360
tcaatgtcaa cctctctatc ttctctctca acaagaagtt tttgcgggaa tgacagagcg 420
aaaggggtgct acccaagccc ctcttacctc tctggatgct ttctttaaca ctaactcacc 480
actgtgcttc cctgcagaca c 501

```

&lt;210&gt; 485

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

```

<400> 485
cgcactcttg gaacattctt tctttcaaca acccaaggca tgcctctatc tccttttgag 60
gtttccctct aagtgttacc tctaagatag gcttttcctg gacactctat gatggaacct 120
ctaggatatt ctctattgtt ttatgcttat ttigtatatt gattcctaga attttaaata 180
cattatataat catataaaat aaacctttaa atattgaaat gaaaagataa aaatacatat 240
actaagtgaat taggtcaaaa gtgtgagatc atcttgaaca ttatcttgaa gagaagatag 300
caattttacct tctgctcaga tcatgggtga cgatatcaca acctgcctag aataactctc 360
cttttctgaa ccaattattc actacttttg tcttccaatt aaatataggc ctgacttcaa 420
atatcataca ttagtttctt ttgtttatgt aattgaatta tataacatat attcattaga 480
gootattttt tttaaaattt ttgt
504

```

<210> 486

<211> 501

<212> DNA

<213> Homo sapiens

<400> 486

```

gagaggtcac tatggcgccct ttctgcagga cgagtgggac ctgctccaaa gaatgatttt 60
gtctggccacc gagaaaactct ctgttccctgt cacgtgcaaa atccgtgtctc tcccgagagt 120
tgacaagacc gtgaggtagc ccagatgct ggagaaggcc ggctgccagt tgcgtacggt 180
gcacggacgc accaaggagc agaaggggccc cctgtcgggt gcagcgtcct gggagcatat 240
caaggctgtg cgaaggctg tgcccatccc tgtgtttgct aacgggaaaca tccagtgcct 300
gcaggacgtg gagcgctgcc tccgggacac ggggtgtgcag ggcgtcatga gcgcagaggg 360
caacctgcac aaccccgccc tgttcgaggg ccggagccct gccgtgtggg agctggccga 420
ggagtatctg gacatctgac gggagcacc ctcgccctct tctacgtcc gggccaccct 480
cttcaagctg tggcaccaca c
501

```

<210> 487

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(501)

<223> n = A, T, C or G

<400> 487

```

accattattt agcagcaaaa aggaaagtgt gaagacatta acaggaactg gtttaattgta 60
gtccttatct gaaaaggaca gattgaatgc agccaaatta tggcaaagaa atcagtagga 120
caaccctcat aaagggtagt tcttttaaaa aaaatttctt tattggcaac aacataaaag 180
atatgaaaga atcactcata atttatcagc ataacatagc tattctcatt ttgtcaattg 240
actttttagt tcttgaccaa atgtaatttt tattagttgt gattaactga ttttgtgctt 300
tttttaaaaa aaaaaaaaaa ctagaataag acatttggtt tgttaattat tataaatgac 360
tgtattcatt ctgtttatgt accataattt tggatgttcc tacgatgtta aacttttagg 420
ttgtttttaa ttgtttgttc ttatagacaa ctctgtaagg gnttttaact gcttttatca 480
ggagaatgac aaagaagtcc t
501

```

<210> 488

<211> 148

<212> DNA

<213> Homo sapiens

<400> 488

```

attctaagga tgaatggct acagagcaaa ctgcagctga gagaaaactg cttggagttt 60
ggacagaggt ggaattgagt gtccacaggc cagctgagga ggtggtaccc agcactctat 120
gaacctctcg ctcaagtgcg cctggagt
148

```

<210> 489  
 <211> 501  
 <212> DNA  
 <213> Homo sapiens

<400> 489  
 gctgtggatt cccctccaag tggaggagga tgggcaggct ggggatcctg gggcaaatct 60  
 ctgctgtgct cagcatctgc cacagtaggt catggattga cggcagtc aa gaaaaagca 120  
 ggagccactc tacggattca tgggtgtaaat tctggatcct ctgaaggagc ccaaccaa 180  
 actgaaaacg gaggccctga aataacagat gcagccacag atcaggggccc tgcagaaa 240  
 ccaccacttt ccccttcctc agcctctcgg ggtatgctgt ctgccatcac caatgtggtt 300  
 caaaacacag gtaaaagtgt cttaactgga ggccctgatg cgttggaatt catcggaag 360  
 aaaacacatg atgtccttgc agaaagtgc cggggttta agcggacc aa gacgctcatg 420  
 gagagaactg ttctctgtc tcagatgtta agggaagcta aggagaagga gaagcagaga 480  
 ctggcacagc agctcacgat g 501

<210> 490  
 <211> 482  
 <212> DNA  
 <213> Homo sapiens

<400> 490  
 attgcaaat gaaagtggac aaagacttaa ggtaaacctg ctctcatgag tggaatgctt 60  
 ccaaatctgt gaaggaggac tttagggcag agttcactaa ggaggtctgt gcttatagat 120  
 cagtgggctt gaaagaagtt tctctaggtt ctggttgtgt gctgtacgag gtgtaggtag 180  
 taataatact ctgtgcagcc acagtgaagc cccaagctag cgggtagtag ggactgacct 240  
 tgtacaggca gcatggagaa actaagacag agtgtcctgc ccaagtgatg gcaactggga 300  
 gcagtcactc aggtttatct ccaccagggc caagaaagaa aagaatgag gcaactgaaa 360  
 attccataca gatagatacc aatatccaag gtgcttggct ttagcggtgt gggaccacag 420  
 ttaaggctct tgggtgggaag gtgggaggtt ttttcagcat gagatagggt tcaggctgtg 480  
 aa 482

<210> 491  
 <211> 483  
 <212> DNA  
 <213> Homo sapiens

<400> 491  
 cgctctcccc cgtgatccct ctctcgctaa ccgtaggcgc ttttctgtga gggccggggt 60  
 tttcacagac ttcgcttttc taaccacgaa cagtgcctgt tggttcgag ggcagcaag 120  
 gagagccccc cccccgcgc ccgccccgcg ccgccccccc gccgcttttg gatcccgagg 180  
 actccgcccc gcccgccctc cccaggcatg gcgcgcgtgc gcttctcgc caatctgttc 240  
 ttgctattcc ccagatctcc cggcctcccc gcgcgggtgc gggcccgagg cagctcgggc 300  
 ttcgaggccg tcgaggtggc ctggccgtac cgggagacgc ctgaggcgct gccgcgcgc 360  
 gcgcgagaag cggggtcgc gcttgtact atcaacacgc ccccgaggga ccaagagaag 420  
 ggggaaatgg ggctgggggc cgtccccggg agacaggcgc ccttcgcaga gggactggag 480  
 cag 483

<210> 492  
 <211> 266  
 <212> DNA  
 <213> Homo sapiens

<400> 492  
 acctcatctg ctttgccttg gcatgtgagc cttgcctaag ggggcatact tgggtcccta 60  
 gaaggcccta gatgtggggc ttctagatta cccctcctc ctgccatacc cgcacatgac 120  
 aatggaccaa atgtgccaca cgtcgcctc cagtgcctct gactctgtcc 180  
 ccatgggctg gtctccaaag ctctttccat tgcccaggga gggaggttgc tgagcaataa 240

agttttcttag atcaatcaaa aaaaaa

266

&lt;210&gt; 493

&lt;211&gt; 483

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 493

```

gccgctcgcg ctaggagagc gggcttcggg cacttgacat ggcggcagtg gcggcgactg 60
cagcagcgaa ggggaatggg ggcggcggtg gcaggggcgg ggcgggggac gccagcgga' 120
cgcgaaagaa gaaggggcccg gggccctggg ccacggcgta cctggtcacg tacaatgtgg 180
tgatgcagcg cggttgctg gttatagcgg ttggtctggt ccgagcatac ctggctaagg 240
gtagctacca tagcctttat tattcaattg aaaagccttt gaaattcttt caaactggag 300
ccttattgga gattttacat tgtgctatag gaattgttcc atcttctggt gtccgtgact 360
ctttccagggt gatgtcaaga gtttttctaa tatgggcagt aacacatagc gtcaaaagag 420
tacagagtga agacagtgtc ctccctgtttg ttattgcatg gacgatcacg gaaatcatcc 480
ggt

```

483

&lt;210&gt; 494

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 494

```

gtggctattt tcatggaata tcttttatca gcctttcagt tttaatttat ttgtgtcttt 60
ggatctaagc tcagttttgt ttggacaatg ttagttttga tcatgatttt aaaaaatcta 120
ttctgaagct ggggtgttca cactgtgaat ccagcactt ttggaggatc tcttgagccc 180
aggagtttga gactagcctg gtctacaaag tgagactctg ttctacaaa aataataaat 240
aaatagttgg gtgtggtggt atgcgcttgt ggttcagct acttgggagg atgaggagg 300
a

```

301

&lt;210&gt; 495

&lt;211&gt; 496

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 495

```

cgaagtgaag gtagggggcc cgtacgcgcc cgcctgactg tcgccagcag ctccctggcg 60
gcccccacgc agccgcgcct ccctgaggcg cgggaggccc gcgcccgcg gctcgctgtg 120
cgtgggaggg cgcgagcgaa cgcggcgag gagcgccga gccgctgaag aggagctggg 180
cgccggcgcc ccggccgcgc tcggcccgcg gatcgctcc gcccggtctt cgccggcccc 240
ggccctggcg gagatgccgt gtggggagga ttggctcagc caccgcctgg gaatcgtgca 300
gggattcttc gcccaaatg gagttaatcc tgactgggag aagaaagtaa ttgagtattt 360
taaggaaaaa ctgaagaaa ataagtctcc taagtgggta ccatcactga acgaagtccc 420
ccttcattat ttgaaaccta atagttttgt gaaatttcgt tgcgatgattc aggatattgt 480
tgacctgag ttttac

```

496

&lt;210&gt; 496

&lt;211&gt; 494

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 496

```

aaactatata aaaagtgtatt tgtacagaac tttatttttag ctctttttta aaaatgtatt 60
gcatggttag aaaaacggcg ggacagccag gggagggaag ggctcttagg gaactttgca 120
ctttctatcc ctttgtacta tgcactgccc tattgattct acacccaata atgatattac 180
ttgaaccatc ctgtaagaaa ctgcttcgga aattcatttg tgtgtatgta aataacacaa 240
catagaacaa ggaagggaaa aaagtctgca gtaatgcacg tatttttttt ctttctgttt 300

```

```

tattttcgggt ttgtctttaa gtcccttttat ttttaattcc ctttttggtt ttcttttttg 360
gtttttggttc cttttggggtt tatgggtgcc ctgatactcc agcagagatc agaaggctac 420
agatccattc tatccatccg ttatgttggtt ttgccatccc agcttgaggt gtctttacaa 480
agataataac agtt                                     494

```

&lt;210&gt; 497

&lt;211&gt; 184

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 497

```

gcgcgcgcgc gctggcaggg tgtgcgtgag ttgggtggcg gccggtgtg cagagacgcc 60
atgtaccggc tcctgtcagc agtgactgcc cgggctgccg ccccgggggg ctgggcctca 120
agctgcggac gacgcggggg ccatcagcgc gccgggctgc cgctctcgg ccacggctgg 180
gtcg                                     184

```

&lt;210&gt; 498

&lt;211&gt; 471

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 498

```

tcttactaca aatggagatg gctattatga aacagcatga gcatgagcct tttatctttt 60
atacttagtg atatactttg cttgaaaatc actcagcaaa gtagttcaca tgaatgtgat 120
catatttgaa gtgtggtttt tctcaaaatc attgacttta aggagctcat ttctgaacaa 180
aaagggtttc tctgtggaaa aatcaatcac tgccaggatt ctctcatctt tgtactattt 240
tgtataaatt aatttgttca ctctctcac accagcaagt gtttacaggt gcctctggat 300
taaaacaaaa ttgatttttaa aatttttatg taagtcaatt tgtctatgat gccactttta 360
aaaggaaaaa gcaattgcgt aatggcttat atccttattt aatgtacctt tttgtgttct 420
aataattggt tgaatgtttt attcagctta aaactttacc atgaagtcata a 471

```

&lt;210&gt; 499

&lt;211&gt; 478

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 499

```

aggtgggaaa agcggaggag gacgcccagg aggaggcgcc gccggcgccc gggaagttaa 60
aggtctgcga aagttcagcg gcggctgcgg gcgcgcagcc ccgggctagc ggcagacgag 120
ccgcgaggcg cgctcccgcg ggcagcgagc ccaggccggc tatggtcccc gggtccccgc 180
cgccccccag gtgcccgagg cccgcccagg cggtgcgcga gggtaacccc acctccccgc 240
gcgggtcccg cccctggctc ccagctgcgg gcgaccgctg accgagcccc gcgccccagg 300
aggaggaaaga aaccaggggc cgttcccttc ccgaggacgg cggcgcttca tcccgcagcc 360
cagagggtctc ggctccctcc ggcacccgcc cggcccggtc gctcccggtc cctcccggcc 420
atggggagct gcgcgcgcgt gctgctgctc tggggctgca cggtggtggc cgcaagga 478

```

&lt;210&gt; 500

&lt;211&gt; 495

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 500

```

gggggcttct ggcttggtgt ggaccaggag ggggcagaag gcacctgtc gtggctgggc 60
accgtctctg cggctgctgc tagcctctgt gtctcgttca acgcatctca caccacgaag 120
gtgctccggc cgtctggagc cagcatctgg cgctgactt tctacaacaa cgtcaacgcc 180
tgcgtctctt tctctccctc gctcgtgctg ctccgggagc ttccagccct cgtgactttt 240
gccagctggc gcagtgccea ctctggggg atgatgacg tggcgcgctt gtttgctttt 300
gccatcgctc acgtgacagg actgcagatc aagttacca gtccgctgac ccacaatgtg 360

```

```

tcgggcacgg ccaaggcctg tgcccagaca gtgctggcgg tgctctacta cgaggagacc 420
aagagctccc tctggtggac gagcaacatg atggtgctgg gcggctcctc cgctacacc 480
tgggtcaggg gctgg                                     495

```

```

<210> 501
<211> 494
<212> DNA
<213> Homo sapiens

```

```

<400> 501
ctgcgggtg gttggtggtg agatgacgac cttagtgtg gataatggag cttacaacgc 60
caaaatcgtt acagccatga aaatgtgtcg gttattccta attgtcagtt ccgggtcaaaa 120
acagcaogct ttaaaaacttt tactgccaac cagatagatg aaataaaaaga ccttctctgga 180
ctctttttaca tcctcccttt tcaaaaaggcg tacttggtga attgggatgt tcagagacaaa 240
gtttgggatt accctttttg aaaaagaaatg tatcaggttg attttttaga tactaatata 300
attatcactg aaccatactt taacttcaact tcaattcaag aatcaatgaa tgcaattcta 360
tttgaagaat accagtttca agcagtatta agagtaaatg ctggggctctc cagtgcacat 420
aggtatttcc gagataatcc ttccgaatta tgctgtatca ttgtgtatag tggatatccc 480
tttacacata tagt                                     494

```

```

<210> 502
<211> 479
<212> DNA
<213> Homo sapiens

```

```

<400> 502
ttgtataatg ctgaatgtgt ccagagggac aagtttgacg aacctcatat tggtatatta 60
aagaaataat aaaaataaaaa agcacttttag gttattttat ctttaaccog attgctgcaa 120
tttcttttgt gtgtatataat acatatataat actttccaca aagttttatt tttgtctcag 180
aataaaaaagt taaattgagg tgtgaaaaga aaagcactta ctttggtgca atatgtgatg 240
cttgatggtc gttgtcccat gtggccctgg cctggcagcg ttttcccgct caatcagccc 300
tgtgtctgta gattgtccat agggaaacac tattatgcac tctcagcaac cgctcaatct 360
atgcaagcct tcctgtgtgt ccccaggcgg cccctcagg ctctctgaag aactgctgtg 420
ggtcctgttt tctgtgact gttgaggccc tttttcatca cttcttggtc tctcgccat 479

```

```

<210> 503
<211> 451
<212> DNA
<213> Homo sapiens

```

```

<400> 503
ttgtgggcgg ggtgggttct ctaactctgt tctgtctgcc tggttcatct gbtgtgcgatg 60
gctccggact cggatccctt ccctgaaggg ccgctcttaa agctgctacc cttagacgct 120
agagaccggg gcaaccagcg ctgcgcgcctg ggcccgccgg cctccacgc cctgggcgg 180
cgcttggtct cggcagtgaa gatctcgcta cccgacggcg gctcctgctc ctgcaactgcc 240
tggcctcgcc ggagcggagc ggacggcttt gtgcagctgg acccgctgtg cgcgagcccc 300
ggggcggcgg tcggggcgct gagatcccg aggagtctca gcttgaatcg cctcctccta 360
gtgccctgic cgccctcgcg gcgcgtcgcc gtgtggccgg tgttgcgaga gcgggcaggc 420
gcgcccggtg cccggaatac agcccggtg c                                     451

```

```

<210> 504
<211> 462
<212> DNA
<213> Homo sapiens

```

```

<400> 504
cagtggggaa ggggagagat gccaggtgg tcagtatcct gactttcaga ggcctttttt 60
tgtttgtttt aatttttgtct agattgatat taaaaactca tgtggaggaa ctcaaggaa 120

```

```

gtttagaaga ccaaaagtcc ccaatgacag gaacaaaagc aaccaatttt taactttctc 180
ttctcattcc tgttttcatt gatttccacc atgtagtctt tttgctcagg aagtctttgg 240
ggaaaattag gatctttgaa gctctgaaat aggtgatcag gttagtgggt tctgtcagct 300
gtctaagagg ttggaaaaatg aactactcaa gatagtcacg aaaatactga aagtttgatt 360
ttctcttcca tatttgaatt aattttttct gtttgactgg aagggggttt tgtataacta 420
aaacctcagc gcataaaggga gatttaaaag gagccatga tt 462

```

&lt;210&gt; 505

&lt;211&gt; 136

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 505

```

tcgattatat cacacatttc agttgggagg ttgtctcaac ctgtgaccac catctgagtt 60
agctggcaga cttctaggag gtccgtgtctg aggtagaatc agaaatggct tccctccttc 120
tcccataaaa aaaaaa 136

```

&lt;210&gt; 506

&lt;211&gt; 466

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 506

```

ggggtacaga gacagcagcc tgcggagcgt tctaggcagg acaggggcagc aaacctgaca 60
tgcggagctg ggggcagggg taatggggcc agggggtaat ggcagggtgag gccatggcct 120
agagggttgc catgcttggt gcaggggagg agaggcccag gtgtggctgc agtggcagca 180
ggagtcagtg ttgctgtgcc cagtgggatg ttgtcagaga atggacctgg ctgctgggaa 240
aggtgattgt gtttgtctga gccacactgg actcttctct gaccagcaag cacattctgg 300
agatgcgggg cagagacgag gcctccgtga gaacctttga ggtgtgaggg ccttgatctg 360
gggtgcagcc tccagctttc tgottacaga gcaggacctg caggagctcg ctgactgcct 420
gcacagtgga aggaagacct gttttcttta ctttcttga ggagaa 466

```

&lt;210&gt; 507

&lt;211&gt; 101

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 507

```

atgattttaat tttttaaact gtagcaattg gatagataat tttatttgaa attttacaca 60
ctgaaagctc taaataaaca gatacattca cattcaaaaa a 101

```

&lt;210&gt; 508

&lt;211&gt; 242

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 508

```

gacaatgcaa gtaacctcaa atgagagtgt ggaaaggcgg gaaagcagcc agagcttcat 60
tgttatgaaa aaagagttaa atgtgctctg ttgaagagtt gaagaatgaa caaaggatat 120
ttagtttgaa tggaagctca gtaatgagaa atgagaatgg ttgagttctt aaaagaagca 180
agtaaagaag aggattttgt ggctactatt ctcatcagtg gaatctcatw ccacctctgc 240
ct 242

```

&lt;210&gt; 509

&lt;211&gt; 101

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<400> 509  
 cctttgctcc ctttttccaa tttcttattg catatctttc tgtattacaa caaaatgata 60  
 tgcaataaga aattggaaaa agggagcaaa ggcgaagggg y 101

<210> 510  
 <211> 461  
 <212> DNA  
 <213> Homo sapiens

<400> 510  
 gcaggttcgg gaccatgagt tggattcctt ttaagattgg gcagcccaag aaacagattg 60  
 tgcccaaaac agtggagaga gactttgaaa gggagtatgg aaaacttcag caccatgtca 120  
 aaatctgccg tgaagatata cttggactta ctctccaatc cctctgtgga gcaagaccag 180  
 gaccttctga acatgggtgac ggcctctggac acggccatga agcggatgga tgccttcaat 240  
 caggaaaaag tgaaccagat ccagaagact gtgatcgagc ccttaaaaaa gttcggcagt 300  
 gtcttccoga gcctcaacat ggctgtgaag aggcgggaac aggccttgca ggactacagg 360  
 aggtgcagg ccaaggttga gaagtatgag gaaaaggaga agacggggcc agtgcgtggc 420  
 aagctccacc aggcacgaga ggagctgcgg cctgtgcggg a 461

<210> 511  
 <211> 461  
 <212> DNA  
 <213> Homo sapiens

<400> 511  
 ggctttctga tttttctaaa attgacctgg aatcaaccat tgacatgtcc tgtgctaaat 60  
 atgaattcac tgatgccctg ctgtgccatg atgatgagct ggaagggcgc cggattgcct 120  
 tcactcgtga cctgtttctc ccctgggaca ggagcatggg tggtaacctg gacctgtaca 180  
 gcattgatga acactttcag ccgaagcaga ttgtcaagtc tcttatccct tcgtggaaca 240  
 aactggtttt ctttgaagta tctcctgtgt cctttcacca ggtgtctgaa gtgctgtctc 300  
 aagaaaaagc acgtttgtct ataagtggtt ggtttcatgg tccatcatga actcggcctc 360  
 ccaactactt tgaacccccc atacctcgga gccctcacat cccacaagat catgagattt 420  
 tgtatgattg gatcaacctt acttatctgg acatggatta c 461

<210> 512  
 <211> 686  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(686)  
 <223> n = A,T,C or G

<400> 512  
 actgacctga aggagacctt agagtccttt ccccttttga gtttgaatca tagccttgat 60  
 gtggtctctt gttttatgtc cttgttccta atgtaaaagt gcttaactgc tctctggttg 120  
 tattgggtag cattgggata agattttaac tgggtattct tgaattgctt ttacaataaa 180  
 ccaattttat aatcttttaa tttatcaact ttttacattt gtgttatitt cagtcagggc 240  
 ttcttagatc tactttatggt tgatggagca cattgatttg gagtttcaga tcttccaaag 300  
 cactatttgt tgtaataact ttctctaaat tagtgccttt aaagggaaaa tgaacacagg 360  
 gaagtgcctt tgcatacaat aatgttgtct tgttaagtat tcattataaa tacatgcctt 420  
 ctatatggaa catggcagaa agactgaaaa ataacagtaa ttaattgtgt aattcagaat 480  
 tcataccaat cagtggtgaa actcaaacat tgcaaaagtg ggtggcgaata tctcagtgctt 540  
 aacacttttc tagcgttggtt acctcgccgc gaccacgctg gaattccgga aggcctgtgc 600



```
ctangatcca gtgtggtgga attctgcaga tatccagcac agtggcgngc gctcgagtct 660
aaanggccgc tttaaccgc tgatca 686
```

```
<210> 513
<211> 429
<212> DNA
<213> Homo sapiens
```

```
<400> 513
catgaacgac acogtaacta tccgcactag aaagttcatg accaaccgac tacttcagag 60
gaaacaaatg gtcattgatg tccttcaccc cggggaaggcg acagtgccta agacagaaat 120
tcgggaaaaa ctaggcaaaa tgtacaagac cacaccggat gtcattcttg tatttggtatt 180
cagaactcat tttgtgtgtg gcaagacaac tggctttggc atgatttatg attccctgga 240
ttatgcaaa gaaaaatgaac ccaaacatag acttgcaaga catggcctgt atgagaagaa 300
aaagacctca agaaagcaac gaaaggaaac caagaacaga atgaagaaa tcaggggggac 360
tgcaaaaggc aatgtgtgtg ctggcaaaaa gccgaaggag taaagggtgt gcaatgatgt 420
tagctgtgg 429
```

```
<210> 514
<211> 346
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1) ... (346)
<223> n = A, T, C or G
```

```
<400> 514
aaaactttct ctacttatatt agttttntcc tctgagtcca accgctgctg gattcgtttg 60
gcataacttt gtgccatgga gttaaatgata gataggatga agtaacacac catgacaacg 120
accaaacttt caaacatcca ggacaaccag ttttctccct gtgggtgtgcc catttcgctt 180
ttgtggtgaa gcttctgcgc ttgagcctcc aggtactcct gaaatggctt ctgcagagat 240
ggacctatgc cggggacagc actggaagca gggtagagta gcccaaagaa aaagacacat 300
ttgggaagaa aagcaggaaa aacgttaaa gaaatgtact taccac 346
```

```
<210> 515
<211> 549
<212> DNA
<213> Homo sapiens
```

```
<400> 515
ctgaccagga ctgtgaagat gcggttccgc tgcgaagatg gggagacatt ttccaggaa 60
gtcatgatga tccagtctct caaatgcaac tacaactgcc cgcattgccaa tgaagcagcg 120
tttccctctc acaggctgtt caatgacatt cacaaattta gggactaaat gctacctggg 180
tttccaggcc acacctagac aaacaaggga gaagagtgtc agaatacaga tcatggagaa 240
aatggggcgg ggtgtgtgtg gtgatggaac tcattgtaga aaggaagcct tgctcattct 300
tgaggagcat taaggatctt cgaaactgcc aagggtgtct gtgcggatgg actaatatgc 360
agccacgatt ggagaatact ttgtctcata gtattggagc acatgttact gcttcatttt 420
ggagctttgt gagttgatga ctttctgttt tctgttttgc aattatttgc taagcatatt 480
ttctctagcc ttttttccct ttgggggttct acagtctgaa aagagataat aagattagtt 540
ggacagttt 549
```

```
<210> 516
<211> 382
<212> DNA
<213> Homo sapiens
```

```

<400> 516
ccgctcgtca gactccagca gccaaagatg tgaagcagat cgagagcaag actgcttttc 60
aggaagcctt ggacgctgca ggtgataaac ttgtagtagt tgactttctca gccacgtggg 120
gtgggaccttg caaaatgata aagcctttct ttcatctcct ctctgaaaag tattccaacg 180
tgatactcct tgaagtagat gtggatgact gtcaggatgt tgcctcagag tgtgaagtca 240
aatgcagccc aacattccag ttttttaaga agggacaaaa ggtgggtgaa tttctggag 300
ccaataagga aaagcttgaa gccaccatta atgaattagt ctaatcatgt tttctgaaaa 360
tataaccagc cattggctat tt 382

```

```

<210> 517
<211> 323
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(323)
<223> n = A,T,C or G

```

```

<400> 517'
acgagcgtag gacgatgctt ctctntgtgc agcctgcaac tgagtcagga ttgaatactt 60
ggaccocagg tctggagatt gggatactgt aatgcttctt tgttattata acataaaagc 120
accactgttc tgttcatttc ctagctgttc taattaagaa aactattaag atgagcaacc 180
acatttagaa atgtttattg acaggtcttt tcaaataatg cttttctaat taatagccaa 240
agatttcata tctaactttg taaccagaat tatacagtaa gttgacacca cttagattta 300
aaggcagaca gttttgcttt agt 323

```

```

<210> 518
<211> 605
<212> DNA
<213> Homo sapiens

```

```

<400> 518
ctggataccg agcgtggggc cccacactgt ggaacaaacc cacagcttgc tcaggatcca 60
tcccagaatc agcagacatc aaatccaaac cagagttcag aagatgtgaa gccaaaaacc 120
ctcccgctgg ataaaagcat taaccatcag atcagagctc ccagtgaaag gcggaagtct 180
ataagtggaa agaagctgtg ctcttctcgt gggcttccct tgggtaaaag agctgcaatg 240
atcatcgaga cctccaatct ctattttcac atccagtggt tcagggtgtg aatttgtaaa 300
ggccagctgt gagatgcagt gagggtggac gatgttagga ttogaaatgg tctcctgaac 360
tgtaatgatt gctacatgag atccagaagt gcggggcagc ctacaacatt gtgacacggc 420
tttcaagctt cgggataact caccattttt ttaactgagag tgtccccctg caactgctta 480
acaaaaatcc aagctcaggg gcttctcagc atttaccata tttctgaaag gctcttctga 540
aaggtgggat ctgtctcttc gtacgacagt gttttatgtt ttccgtgtta ttggtttggg 600
ttttt 605

```

```

<210> 519
<211> 462
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(462)
<223> n = A,T,C or G

```

```

<400> 519
ctgctgttca tgncccttgc agtcttttgt gcaaaataag gcatattnga gctccacatt 60
aaccttgagg caggcgntca ctgtctctgc atgtgttanc agngcacgtc ctcttccccc 120

```

```

ttggtgtggt agcctngnan aggctgccca tacttatcca cacaccagca naagccccgc 180
ttcctgcott tggaaaggcg acaactgott ttcttataaa atcccttctt gtcacagttg 240
ggaatgtgna caccocctggg actcagcaca ttgaggaact tcaagtgtat cagtgtgnct 300
tcaatttctc tacggcangn accatattct gtctccgcgt tggactcgga ggagaagttc 360
tgggtatctg tgctctgaga ctgctagtca actttgtagc gctggctgnc tttagcatgc 420
cctttcttga tgatgantat ctttgaatgg aggggttgga ac 462

```

&lt;210&gt; 520

&lt;211&gt; 565

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 520

```

actcgtaata aatatgcacg cggaacaag ataaaaggct acacctctgc aggcattcta 60
caaaaaatgtc tcaagtttta tatactctgc agcattttctg tgcgggggca gaaggggctg 120
ttgtgtattt tctgaagtgc tgtgacaaaa ggtcctttca catttctttg gagcattttt 180
gaaattgtctt aactataatt aaacaactta agaaaagtaa caccaagctt taaagcattt 240
tttgctttgc tgtcattggg ctttatccaa tacagatcaa catatcatcc agcacagcca 300
agcaccact gaggccaagc agccttgttg gacatggggc ctgtcagagc agggcctact 360
ttcagttaaa tactttggag agtccaggat tctgtctctc tccctcaaca agattaatgc 420
cataagggaa gttgcaagcg tgttagaaac atttttaacc tgaaagttaa gtgaacagaa 480
atattttttt ttccgagacc tctgctatgc accataatat taccatatca ggggttttag 540
cttcaagttt gaaaaacaga ttggt 565

```

&lt;210&gt; 521

&lt;211&gt; 127

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 521

```

acatggctga cgtcaccgtc cagtgcacaa tcaaaaaaga aagaagaaaa aaccccaaag 60
aaagaggatt tttcagtggg gaacatgggt ggctgattag gcttctatta gattacattc 120
atttcac 127

```

&lt;210&gt; 522

&lt;211&gt; 642

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(642)

&lt;223&gt; n = A, T, C or G

&lt;400&gt; 522

```

actatgtttc gtaaatataa taggtntggc ccagaagacc cactcaattg cctttgagat 60
taaaaaaaaa aaaaaaaaat aaagaaaaat gcaagtttct tcaaaaataa agagacattt 120
ttcctagttt caggaatccc ccaaatcaact tctcatttgg cttagtttaa agccaggaga 180
ctgataaaa ggtcaggggt ttgttcttta attcattaac taacattctc gcttttatta 240
cagttaaaat gttcaagatg taacaactag ttttaaagggt atttgctcat tggctcggct 300
tagagacagg aagacatagc agcaataaaa aaaagattct tttgcattta ccaatttagc 360
aaaaatttat taaaaactgaa taaagtctgt ttcttaagtg cttgaaaagc gtaaaccaaa 420
gtgcacttta tctcatttat cttatggngg aaacacagga acaattctc taagagactg 480
tgtttcttta gttgagaaga aacttcattg agtagctgtg atatgttcga tactaaggaa 540
aaactaaaca gatcaccttt gacatgcgtt gttagagggg aataagagag ggctttttat 600
ttttctgttc atacgagtat tgatgaagat gatactaaat gc 642

```

&lt;210&gt; 523

```

<211> 244
<212> DNA
<213> Homo sapiens

<400> 523
ctgaaggagc tgatccagaa ggagctcacc attggctcga agctgcagga tgctgaaatt 60
gcaaggctga tggaaagactt ggaccggaac aaggaccagg aggtgaactt ccaggagtat 120
gtcaccctcc tgggggccctt ggctttgatc tacaatgaag ccctcaaggg ctgaaaataa 180
atagggaaga tggggacacc ctctgggggt cctctctgag tcaaatccag tgggtgggtaa 240
ttgt 244

<210> 524
<211> 407
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(407)
<223> n = A,T,C or G

<400> 524
acgttagtgg tgatgtcacc caccctnnng ctggggccga ggatgctctc attgtgcact 60
gcgtagatga ctctggccac tggggcagag gtggtttatt tacagctctg gaaaagcgat 120
ccgctgagcc aagaaaaata tatgagctgg ctgggaaaaa gaaagacctg agtttggggag 180
gtgtcctttt atttctctgt gatgataaag aatcaagaaa caaaggggcaa gatttgttgg 240
ccttgattgt ggctcagcat cgtgatcgtt ccaatgtcct gtctggcatt aagatggcag 300
ccctagaaga gggcctgaag aagatatatt tagcagcaaa aaagaagaaa gcaagtgttc 360
atcttccacg tattggacat gccacgaaag gttttaactg gtatggt 407

<210> 525
<211> 276
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(276)
<223> n = A,T,C or G

<400> 525
acacaggagg caacgtgttt cacatnatag acttcacttc caactccttg gaatgttcat 60
ttctttggct tacaggagag actagacagg aaggccaggc aatgcttagg caactaaaat 120
gaggttgggg gtaatgctaa cgtcaccctc acagggatgg ccacggggac tgttattcgc 180
aagctgtgtt tctagacctg tttagctggaa gcatggtgag caccatttct ggacgctcag 240
gcgctgtcgg gcttcagtcg tctccaccac acaggt 276

<210> 526
<211> 288
<212> DNA
<213> Homo sapiens

<400> 526
acaattacc accactggat ttgactcaga gaggaccccc agagggtgtc tccatcttcc 60
ctatttattt tcagcccttg agggcttcat tgtagatcaa agccaaggcc ccagggaagg 120
tgacatactc ctggaagtgc acctcctggt ccttggtccg gtccaagtct tccatcagcc 180
ttgcaatttc agcatcctgc agcttcgagc caatggtgag ctcttctctg atcagctcct 240
tcagctcctt ctgtctcagg gtgtgcttgt caccctccct gccggagt 288

```

<210> 527  
 <211> 412  
 <212> DNA  
 <213> Homo sapiens

```
<400> 527
actttgagct tattgttttt attctgtatt aaatatatttc agggtttttaa acactaatca 60
caaactgaat gacttgacct caaaagcaac aaccttaag gccgtcattt cattagtatt 120
ctctattctg catctcggtc tgaaaaacag ctctgttgtaa tcacagatc agtattttca 180
cagctaagca cattcggaacc atttcogtgg ttctcoatga gctgtgttca cagacctcag 240
cagggcatcg catggaccgc agggggcgag attcggacca cttaggcctga aatgacattt 300
cactaaaagt ctocaaaaca ttcttaagac tactaaggcc ttttatgtaa ttcttttaa 360
tgtgtatttc ttaagaattc aaatttgtaa taaaactatt tgtgtaaaaa aa 412
```

<210> 528  
 <211> 489  
 <212> DNA  
 <213> Homo sapiens

```
<400> 528
aaatgcaaaa agtcaaaagta ggtaacaggt tggttaattaa agtgtcagga agactggaag 60
agggcaaaaa caagcagagt tccaataagt gtatgaaaaa aaaaatcata actgaagggt 120
taagaaaagt ccccaaaaggc agaatacaca tatgagcagg aggaataaaa agcttttgga 180
tataccaggc agctttctgt acgactcagg ttacacagtg aatttcctca gtttgagttc 240
agaagaattt gaacttatc cagcaaaata ctccaatctt ttattactgt cctcctcccc 300
catcttcttt ctgggcaaaag ggaatgcttg attaggtcca aagctcctgg cagggggagg 360
ggccatgtgt cacagcataa cagacgggtg caagtgcatt actgagcagg ggtcaggttt 420
gcagcaactc tgataggctc acacaatggc ctccatttta cagccccctc ttggaggccc 480
actgatcag 489
```

<210> 529  
 <211> 631  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(631)  
 <223> n = A,T,C or G

```
<400> 529
acttgccctaa agttttttata tctgnntctt ctgctgtaaa tcttcccttc ataaatgaaa 60
attttaataa aatcaactat gtggaaatat ataattaaag gaattcacta actgtgattt 120
tcataattta gggacattct ctcttagtaa gcatgggtgca ttatttacta gagatataat 180
atgcattaaa acaaaaaatg ttttctatca tcatagaaaa gtttgaggtc cagggataat 240
catctctgga tacattattt cctaccgtcg tggtacacac tgaacacatt tgaggcttat 300
gactggttct ttactttaca aatattgttt agacacattt tcaaatgtca caccaatcaa 360
taataataag gaatggattt tatctatatt gacagttctt tcaaccttaa gactgaactg 420
ctacaggtaa gattcaatca catttttcag gagaaagcta ttgagaccaat tatgctttgg 480
ttatctaata ggggtggaat gacttataat gctatttact ccaggcaaaag agaaaaataa 540
acagacatag gatcttgatt tcaacgtagt tctcctccat gtgcatttct ctgtccggtt 600
aggcaatgcc aactggtcca ccagtgaaca t 631
```

<210> 530  
 <211> 316  
 <212> DNA  
 <213> Homo sapiens

```

<220>
<221> misc_feature
<222> (1)...(316)
<223> n = A,T,C or G

<400> 530
acacatttaa atgactcacg agantnaagt ttttttcaaa tatattaaga tcacaccacc 60
ttgttgttta tcgaaagata ttcaaggaga aagatctgac tctccaaact gcactctgaga 120
ttgccacttt aaacagacct catttcaaac atgcaacaac gccacttgga ataaagcttt 180
ggaaatgggtg ctcattcttat tatttcaact caaacagcat agaaagcaag agaagttggg 240
aatttattct aaaatagaat ggaggttgtc atctacagca gcactctca ctcctctgt 300
gccatttita gcaagt                                     316

<210> 531
<211> 296
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(296)
<223> n = A,T,C or G

<400> 531
aaagtatcat ttatttgaaa aacatacatt atcatntgt ttttgatatt tgataatgaa 60
aaaaatcttt gnttgtttat ttctgaaaaa gaactgtatt tagngattat tttagatagt 120
gatattatan cattcatctg tgtgtaaatt atttcatata ggggaagagt ctgatctgta 180
cctatgggtc ttattgaaaa caacattgga tgtgcatttc tgtgatgta tgaatacat 240
tctactttat ttgaaacat ttgccaaact aaactctgta acactgtata acattt      296

<210> 532
<211> 266
<212> DNA
<213> Homo sapiens

<400> 532
acatatgcac caaattccat tttagaagtt tccatatcat ttctatagaa aacaaagttt 60
gaaaacaagt aacattttaa cacagcacgg tattctacca caactgaaac ttttttcttc 120
ttctcttcta caggactcaa caaaatctaa aatatgaact tgctgtagat ttacctcatg 180
caaaagatctt tatgttatct ctgaaaaatga aaaggatggc cttttaagca cattttactg 240
ttttatacta ttatggcaac ttgtgt                                     266

<210> 533
<211> 289
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(289)
<223> n = A,T,C or G

<400> 533
actcagaagt cactttttaa atcancgaca gaaatatttc actaattcaa ctgaggcaaa 60
ttctcttctt agacaaagga cctagaaatt gagcatgcaa aacatcatc cattcatcga 120
ttcaataaat tagccaattt tacogtcatt taattccacc agaagcaaat actagaatat 180
ctagaagtag ttgggtaaaa gaaacattta cattttaata ttgtgtaatg tcataaattt 240

```

gggggctaaaa taacaccagg tcaaatttga tccctttgta tgtgagggt 289

<210> 534  
<211> 293  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(293)  
<223> n = A, T, C or G

<400> 534  
aaaataaaaag gttcttttaca agatgatacc ttaattacac tcccgcaaca cagccattat 60  
tttattgtct anctccagtt atctgtattt tatgtaatgt aattgacagg atggctgctg 120  
cagaatgctg gttgacacag ggattattat actgctattt tccctgaaat ttttttcctt 180  
tgaattccaa ctgtggacct tttatatgtg ccttcacatt agctgtttgc cttaatctct 240  
acagccttgc tctccggggn ggttaataaa atgcaacact tggcattttt atg 293

<210> 535  
<211> 408  
<212> DNA  
<213> Homo sapiens

<400> 535  
acttgaacac ttaaagagaa aaactctaaa taaagtcata gaggggatgg tagagatgac 60  
cacagaaaaat gaccacggag agtattatga agattgcaag attagacatt gatgatgtaa 120  
attactccct ttctagataa aataatccat agatgtttat gaatcatatt tgtatgatta 180  
ttgctgttac tattattttg acacattatt tattattatt gttgtcacta ttattaccat 240  
taagatagca ggcgtaaaac tgtactgggt ccttcagtag tgagattttt tcatagtcca 300  
gctttattta tctccaggat gtttttgtgg ctgtatttga ttgatattgt cttcttctga 360  
ttcttgctaa tttccaaacca tattgaataa atgtgatcaa gacaaaaa 408

<210> 536  
<211> 184  
<212> DNA  
<213> Homo sapiens

<400> 536  
acctctcatc aaggctctgc ctacaggcac atttgtatgt atctctgcac tgatcaccta 60  
ggtcatgtaa ctttttttcta ggctctacct acgatggcat tgtgacataa ctctgcacta 120  
atcatccagc tgatgtaact ctgtcttagg atgtgcctaa attaaccttt tgacgtaacc 180  
ctgt 184

<210> 537  
<211> 311.  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(311)  
<223> n = A, T, C or G

<400> 537  
ccacagttgt atcatatagc atctntaaca ttctatctag gattatctag tatagatctt 60  
actatatttg gggctatggt gtatacaatg ttaacaagaa catatcttct ctgcataatat 120  
gtgtgaatta taaagaaaag catgagaatg actctaagtt caacaaacat ggggtaatct 180

```

ctatgtgtct ccagtgctct ggatgggctc cccagcaagc cttctctct tctgttctg 240
atattactat tcttttttac attgtgctaa ggaggacaaa aggtgagaga tgaaaataaa 300
gccttgcctt t

```

<210> 538

<211> 302

<212> DNA

<213> Homo sapiens

<400> 538

```

aaaaataaaa agcaaaaact cttgtggtac ctagtccagat ggtagacgag ctgtctgtctg 60
ccgcaggagc acctctatac aggacttaga agtagtatgt tattctcgtt taagcaggca 120
ttgctttgcc ctggagcagc tattttaagc catctcagat tctgtctaaa ggggtttttt 180
gggaagacgt ttctttatc gcctgagaa gatctacccc agggagaatc tgagacatct 240
tgectacttt tctttattag ctttctctc attcatttct ttatatacct tcttttttgg 300
gg

```

<210> 539

<211> 396

<212> DNA

<213> Homo sapiens

<400> 539

```

actgtttatt tgctcctct cttcatgcct gtggctggat gtccacacac actataagaa 60
atataagtc aagcctttgt gttaaagcaag aactacagac tccattcttt caccacaaatc 120
atgaatgacc aataaaaaagc aagttattcc agaggaagaa gcagcccttg aaatgttaag 180
gcttaggctt gaaaggtgaa gagcaggaat tctctcttcc aaatcctaga gcataaaacc 240
atgtgtggcc aagtgcagtc agccctcaag ggcacatgcc aagggcagag cagcccatgt 300
agacagcttc ggagggcagc ggggtgtagg gagttcgggg tagctcctca ttaactatatt 360
gttgggtgag taagggggtg aggtccagtg gcaggt

```

<210> 540

<211> 634

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(634)

<223> n = A,T,C or G

<400> 540

```

ccaaaaacaa gatgaccaga ttgnttttna gcctgatgac cctacaggtc gtgctatgat 60
atggagctct catgggtaaa gcaggaaag agtgggaaag agaaccaccc cactctgtct 120
tcataattgc atttcatggt taacctccgg ctggaaatag aaagcattcc cttagagatg 180
aggataaaa aaagtctcag attcaacagg gggaagaaaa tggagattta atcctaatac 240
tgtgacttgg ggaggtcagt catttacagt tagtctgtg tcttgcact ctctgatta 300
ttaacccccc tcaactacct gtttcagatg catttggaat accaaagatt aaatccttga 360
cataagatct catttgaga aagcagatta aagaccatca gaaggaaatt atttaggttg 420
taatgcacag gcaactgtga gaaactgttg tgccaaaaat agaattcctt ctagtttttc 480
ttgtttctat ttgaaaggag aaaattccac ttgttttagc atttcaagct tttatgtatc 540
catcccatct aaaaactctt caaactccac ttgttcagtc tgaatgcag ctccctgtcc 600
aagtgccttg gagaactcac agcagcacgc ctta

```

<210> 541

<211> 221

<212> DNA

<213> Homo sapiens



```

<400> 541
cacacaaagca gcagagacca tgggaaccct ctcagcccct ccttgccac agcgcatcaa 60
atggaagggg ctctgtctca cagcatcact tttaaacttc tggaaacctgc ccaccactgc 120
ccaagtccag attgaagccg agccaaccaa agtttccgag gggaaggatg ttcttctact 180
tgtcccaaat ttgcccacaga atcttaaccg ctacatctgg t 221

```

```

<210> 542
<211> 287
<212> DNA
<213> Homo sapiens

```

```

<400> 542
cctcttctac tatggcagga gatgtggcgt gctgttgcaa agttttcacg tcatogtttc 60
ctggctagt ttcttcatta agtggtctaca tcttaacata tgcatttgggt caagggtgca 120
gaagaggact gaagattgac tgccaagcta gtttgggtga agtttactcc agcaagtctc 180
aggccacaat ggggtggttt ggtttggttt ccttttaact ttctttttgt tatttgcgtt 240
tctctctcac ctgtgtggta tattttttta gcagaatttt atttttt 287

```

```

<210> 543
<211> 274
<212> DNA
<213> Homo sapiens

```

```

<400> 543
acttgtgaaa cacagctggt cttctgtttc gcagacacgc cttcccctca gccacaccca 60
ggcacttaag cacaagcaga gtgcacagct gtccactggg ccattgtggt gtgagcttca 120
gattgtgaag cattctcccc agtgatgtgc ttgtatccga tatctaaccg tttaaatggc 180
tactttggtt tctgtctgta agttaagacc ttggatgtgg ttttaattgt ttgtctcaaa 240
aggaataaaa cttttctgct gataagataa aaaa 274

```

```

<210> 544
<211> 307
<212> DNA
<213> Homo sapiens

```

```

<400> 544
ccaggtggtt gtcttattgc accatactcc ttgcttctct atgctgggca atgaggcaga 60
tagcactggg tgtgagaatg atcaaggatc tggaccccaa agaatagact ggatggaaag 120
acaaactgca caggcagatg tttgcctcat aatagtcgta agtggagtcc tggaaattgg 180
acaagtgtcg ttgggatata gtcaacttat tctttgagta atgtgactaa aggaaaaaac 240
tttgactttg ccaggcatg aaattcttcc taatgtcaga acagagtgc accaggtcac 300
actgtgg 307

```

```

<210> 545
<211> 570
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(570)
<223> n = A,T,C or G

```

```

<400> 545
accttagaaa tttgcaacca cctccctgaa agtcttctcc cactgttatta agtgcaatgt 60
ttatggtaaa tgtagaagca tcatgatgag gacgaagaga acgctgtcgt tcaggggagt 120
attttactac aaaattcagt agtgcaaatc ccttcgtata atagcctgca aagaccttca 180

```

```

gtgtaactgg ngcaatgaac tcccggataa aatgaagcca tacattctcc agatcaactt 240
gcttcgatgtg gatatcatca gttggggacat ttccataacc accagatata cggctatcat 300
gatgttttcc ccacagacct ttgccgtaat gtgccatttc ttctaccaat tcatacacagg 360
cttttttcaga aaatatgggg aaccaaaga catctggaca gggctgttca actatatttt 420
cagtgaaaaa ctttgaataa tcacgggtta tatacttttc cttccagtc acaggatttt 480
caaaaatctg ccagaggtca ttgttataat gggaagtatt gtaattagca gtggataata 540
gccttccaaa ttcattgtcta ttagaaatgt 570

```

```

<210> 546
<211> 589
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1) ... (589)
<223> n = A,T,C or G

```

```

<400> 546
aaaaataactt ttaccaaaag gtgctatttc tctgtaaaac actttttttt ggcaagttga 60
ctttattctt caattattat cattatatta ttgtttttta atattttatt ttcttgacta 120
ggtatttaagc ttttgaatt atttttcagt agtcccacca ctctcatagt ggaaggagtt 180
tggggttctt cctggtcgag gggctgaaat aaccagatg cccccacct gccacatact 240
agatgcagcc catagttggc cccctagct tcacgagtc cactatctgc cagaggagca 300
agggtcctt agaccgaagc cagggaaga agcatcttca taaaaaact tcaagatcca 360
aacatttaatt tgtttttatt tattctgaga agttgaggca aatcagttat cccaaggatg 420
gcgacaaggg cagccaagca gggcttagga tatccagcc taccaatagt ctcatcgac 480
taactaggag ggtgagttg ccctgtctct tcttttttct ggacctcagt ttcccttcagt 540
ggagcttggt aaaaatgcac tacnnttga ttgtataagg tataaatct 589

```

```

<210> 547
<211> 293
<212> DNA
<213> Homo sapiens

```

```

<400> 547
actcctatta ttgactgtag tcaatcaaac ataaaaaggt gaaagtaaaa ttaattttt 60
tacccttatt ttactgacca atatggaagt tcttggtatc ttaaggctg accttctctg 120
tattgtgtaa tgattgaatg tatctaaact gtaataattt gaaactgaca aacataacct 180
tctcagactt acaaaactat gttctttcta aagatacaga tttttattat ttatttttga 240
ctaggaagga ttataaata aatgtaatga aaaatctttg atcttaataa agt 293

```

```

<210> 548
<211> 98
<212> DNA
<213> Homo sapiens

```

```

<400> 548
aaacaaaggt tgagatgtaa aaggatttaa attgatgttg ctggactgtc atagaagta 60
caccacaaga ggtattttatc ttactttttt ttgtaca 98

```

```

<210> 549
<211> 121
<212> DNA
<213> Homo sapiens

```

```

<400> 549
acatgcatat ttcaaagacc tgtaaatggc gtccactttg gattcttaca tgaaacgatt 60

```

```

cagtgcacat tgtaagccta aggaccacgc aaaaggggtt cccacatatt aagtattcag 120
t                                                    121

```

```

<210> 550
<211> 509
<212> DNA
<213> Homo sapiens

```

```

<400> 550
acaatagtat acattttata atgatgaact tataatgatt aagggaacatt tctataaaaa 60
tactacaata gttttatgca caacttcoca ttaaaaaatga gatttcttat ttgtttgtct 120
gttttttactc tgggagtaat acttttttaa ttacctttac atatatagtc actggcatalc 180
tgagaatata caatgatcct ggaaattgca gtaacaaaag cacacaacga ttatagtaac 240
tataagatac aataaaacaa ataaatgtga aagtagattc atgaaaatgt attcctttaa 300
aatattgttt tctacacggc ctatttaaca agatgtttca ttttactgta tatttgttag 360
ttaatataaa tgttgctcta atcagattgc ttaaaagcat ttttattata tttatgttgt 420
tgaaataata tatgaataaa gtaaatgtag ctcccacaag gtaaaactca ttgtaagat 480
tgcactgttc tgattatgta agcatttgt

```

```

<210> 551
<211> 427
<212> DNA
<213> Homo sapiens

```

```

<400> 551
accatgttta tatgattaat ctggggacaa agaattttat agaaaatttt aaacatctg 60
aaaagaagct taagttttat catccttttt ttctcgtga atctctaaag gattatgctt 120
taatgctgtt atctatctta ttgttcttga aaataacctgc attttttggc atcatgttca 180
accaacatca ttatgaaatt aattagattc ccatggccat aaaaaggctt taaagaatat 240
atatattttt ttaaagtatg ttgagaagca aattggcagg taatttttca tacctaaatt 300
aagactctga ctggattgt gaattataat gatatgcccc ttttcttata aaaacaaaaa 360
aaaaataaat gaaacacagt gaattgttag agtgggggta tttgacatat ttacagggt 420
ggagtgc

```

```

<210> 552
<211> 340
<212> DNA
<213> Homo sapiens

```

```

<400> 552
cctcaaggcg gtccaattat ccaacttcag attctacaga aagagtggtt caaaaactgct 60
ctgtcaagag aaatggtcca cagtgtgtgt ggaatgcagc catcacacat tagtttctga 120
gattgcttct gtcttggttt tatgtccatt tctagcatag gcttcaaggc 180
gtcttaataa tccgcttgga aatactacaa aaacagtggt tcaaaaactgc tgtatccaaa 240
ggaaggtgcc actcgtcgag ttgaatgcac acatcacaa gaaagtttct agaattcttc 300
tgtctagatt catacgaaga aatcccgttt ccaacgaagg

```

```

<210> 553
<211> 549
<212> DNA
<213> Homo sapiens

```

```

<400> 553
acttgagctg tgaggtcatc ggaatccoga cactgtcct catctggaac aaggtaaaaa 60
ggggtcacta tggagttcaa aggcagaaac tctgtcctg tgacggggac aacctggcca 120
ttcagaccgc ggggtggcca gaaaagcatg aagtaactg ctgggtgctg gtatctcctc 180
taagttaagg agatgctgag gaatatgagt gccatgcac caattcccaa ggacaggctt 240
cagcatcagc aaaaattaca gtggttgatg cttacatga aataccagtg aaaaagggtg 300

```

```

aagggtgccga gctataaaacc tccagaatat tattagtctg catggtttaa agtagtcatg 360
gataactaca ttacctgttc ttgcctaata agtttctttt aatccaatcc actaaacttt 420
tagtttatatt cactgggtttt acacagagaa atacaaaata aagatcacac atcaagacta 480
tctacaaaaa tttattatat attttacagaa gaaaagcatg catatcatta aacaaaataa 540
atacttttt 549

```

&lt;210&gt; 554

&lt;211&gt; 321

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 554

```

acctaataat atgttaacat aaacataaca acacacatat tttttttcta ccccttggca 60
actgaaaaatg aagttacat tcttaggccca aatttttaga caaagctttc taaaaccatc 120
tttataaagt aaattcagat atgcttacaa taaaagaca taaagattc atcctgagat 180
gaattctgag tcaataaacta aaaaccattt ctaccagtgc atcactacca tgtaattccat 240
tctacgcaag ctctacaat attgagtaa atcctgtctg tcagaaaatg aagacccaat 300
aagtttgcg aagtattcat t 321

```

&lt;210&gt; 555

&lt;211&gt; 322

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 555

```

ctggatcccg agaatactgg aacaatagag ctgcacctta tctcttggtt ctgttttctca 60
gtactttgaa gttataaacta atctgcctga agacttctca tgatggaaa tcagccaagg 120
actaagcttc catagaaata cactttgtat ctggacctca aaattatggg aacatttact 180
taaacggatg atcatagctg aaaaataatga tactgtcaat ttgagatagc agaagtttca 240
cacatcaag taaaagattt gcatactatt atactaaatg caaatgatgc gcttaaccct 300
tgacaaggct aaagaaaact tt 322

```

&lt;210&gt; 556

&lt;211&gt; 286

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 556

```

aaaaaataatg tatctaagaa tgttctaggg cactctggga acctataaag gcaggtattt 60
cgggccctcc tcttcaggaa tcttctgaa gacatggccc agtcgaaggc ccaggatggc 120
ttttgtctgc gcccgctggg gttaggggga cagagagaca gggagagtca gcctccacat 180
tcagaggcat cacaagtaat ggcacaattc ttccgatgac tgcagaaaat agtgttttgt 240
agttcaaca ctcaagacga agcttatttc tgaggataag ctcttt 286

```

&lt;210&gt; 557

&lt;211&gt; 459

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 557

```

acagaagatg aataataatg aaaaactgtg attttttgac tatcacatac atttgtgttaa 60
aaaacaggta aatataatga ctattactgt taagaaagac aaggaggaaa actgtttcaa 120
tgttccagtt taaatactaa gcacaaaaat ataacaaatt ctgtgtctac aataattttt 180
gaagtgtata caagtgcatt gcaaatgagc tcttttaaat ttaagtcca ttcccccttt 240
agccaaagcat atgtctacat ttatgatttc ttctctctat tttaaagttc ctctcgtgtt 300
agttttttaa aaagtttcat catggctgtc atcttggaat ctagcctcca gctcaaagct 360
gagacttcac gcatacatat tctcctttct gggtgcatct tcacctagtt tctccaagta 420
ttcagagtta aatagacaaa cttcttttat atgttccct 459

```

<210> 558  
 <211> 303  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 558  
 aaaaaataaa aaacaagaca acaatttagt agaagtaccn ctgggaggga ggggaggga 60  
 aaaaagata tacaggggca gngtattct ctgtacagag gtgcananaa aatttcacat 120  
 anctttanag aatgccttgt ggaaaaaaaa aaataggccc caatacttgt tactgccttt 180  
 tatcaaaact gtgtgcatga cctgcacaaa taaaatcaca aaacagtgtt gccacattct 240  
 tcaaggaaac aaagcaaaat tttaggggnt tcttttcct ctccttgta aaagtcattt 300  
 ttt 303

<210> 559  
 <211> 232  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(232)  
 <223> n = A,T,C or G

<400> 559  
 aaagcattta ttaagaattt actcaggcat gatggcccat acttgtaac ccagctattg 60  
 ggaaggatga gatgggaggga tggcttgagg ccagaggttt gagaccgacc agccagggca 120  
 acacagttag acccttcttc aaaaaaaaaa aaaaaaaaaa agagagtgtg tgattagaag 180  
 ctaaatagga aagttttgag cttcaagtca gngaggagta aaaaagattt tt 232

<210> 560  
 <211> 336  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(336)  
 <223> n = A,T,C or G

<400> 560  
 ctctgcaaaa ataannataa aaaaataaat aaaaatttaa aaataataaa attcactata 60  
 tacacatata aagaataaaa aagaagtctc agttgcagct atttgtaaaa attaatatoc 120  
 attttttttt atatacggtg aatattgcgc aattatagat ctggattttg aaccacttaa 180  
 tgaagcgcca acaccagggtg ttttgagggtg ttggcattct tcgctgattt ggctgttccc 240  
 aatgtttaca ttatttaaat ttgcaaaaat ggttctgtgc acttgatgn gaaatgctgn 300  
 ccagntttat tttttttatg ttgntatcct tggatg 336

<210> 561  
 <211> 636  
 <212> DNA  
 <213> Homo sapiens

```

<220>
<221> misc_feature
<222> (1)...(636)
<223> n = A,T,C or G

<400> 561
acattatggg ttttattgct ttcttttatg gtagacctgt taatggggaa aaaatacatc 60
aaatcaaatg gaactttata tctgtatggt aaatatagagc acttacctga agtcagtgcc 120
ctggatcata gccctggatc atttcccagt ctgtcctgtg ctgtgtgacc ttggacaagg 180
cgcttcatct ctctgggctt ctattttctc atttgtaaaa caagtggctg cagtagatga 240
tggctgagag cccttctctg tcccagatgc ctgtgtccaa agaccccacc cctctgctgg 300
tcctgccaac gtgttgggtg tataagctgc ttcagatata aaattggttt atctataatg 360
tttgttcatt taatagcttc taaaaggcct ttgtttata cagtgccttt tttctagttt 420
tatggacttg gttactgtaa taatgtcttg tttttagcca tgtaactaca aacagatatt 480
ctcttgatgt cttagttaat ttgcatttga tatatcattg atgagatttt gttgttatgt 540
aatattcttt ggctacgcat ctgtccagca tcttattaac cataactg ngatcattat 600
ttggaatatat gtctatgga aagaataaaa gcatgt 636

<210> 562
<211> 708
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(708)
<223> n = A,T,C or G

<400> 562
acagtccacc ttttgataca tgccatgcct ttgatcaaag aacaggacat aaaaacaaag 60
tcacaatgac attccatagt aaatttggaa tcagaactcc aaatgcaact tcgggctcgc 120
tggagaacaa ctaaggggca ccaaaccctc tgaggtttta cttaaagggt cgctgtatgt 180
ttgccttggg caaaaaggct acctaccag tgctatccag taataactt aaataagcca 240
atacttagat ctactgtaag gcagatgcta attataaggc attaatgaag caaatagtgc 300
cctcagctac tgcagaagaa aagtcocact gaggaagaaga aagtcctgtg atttttaag 360
gcaagtttct aagtgccttc atagtctctat cctctaattc cattaaatcc atactaggag 420
cgtcagtgag ggttttcata gcttttggaa atactttggt ctctgaaactg taattagcaa 480
gaagtaaaaa cagaaaagtc aaacgtcaaa tgtttgcctt gttacctgga ggactaaatg 540
tagatgtctt tagtatactt tgtatgtctt taatattgga agataatttt gtgaatctgt 600
agattttatt ttttcagtct taccttacia atttcttttc tatgaataat agaggactta 660
cngcactctg ccatttggta atgaaaggaa ggcngangat ttgaaag 708

<210> 563
<211> 290
<212> DNA
<213> Homo sapiens

<400> 563
ccagatgctc atccactttc agactttcat ctcttctgcc atctgcaaaa gtcaacagag 60
ctttccggaa gtcaccagat gtttcggaac taatgtcatc tccaagactc ttcttgtata 120
ctgtataata ggcttgagag atatccttca ttgtcctgtg tgtcctgtga tctaagattt 180
caatcaaggc atcttctgtt gttccgcgc ccttcatgga ttctcttagc gtctttgcac 240
caaagactgc tgggtggatc actagggcca ccatgagatg ctcaaagtgg 290

<210> 564
<211> 530
<212> DNA
<213> Homo sapiens

```

```

<400> 564
accaccagat acttaaaagct tcaaaaagac tgccctacc accacaggag gaccagccta 60
accatcagct ccaaagatg gctgtgatg atcttgtgaa gcaattactg agcagatcaa 120
gatctttggg aaggaacact aaagatgttt tgaatgaatt atagtccact ggcattttag 180
tgtatttttt ttctttttta gaaacacaca ttcttaaaaa tgtcatgtta cattcctgca 240
tgtccctttt gatagcatta gtggatccat tggatttctt tttctttttt gtgagacagc 300
ttttagtctt acctgaattt atgtgtgttt ttccgacagt gggttaataat tatattgggtg 360
atgtagcagc aattgtgttg gcagggtttt catatattat tagtaattaa cactaaactgt 420
tggactgact tgtgtcgata gcgctcacgc aagcatgggt aacgtcccta aaaccgcgcg 480
gactttctgt aagaagtgtg gcaagcacca accccataaa gtgacacagt 530

```

```

<210> 565
<211> 450
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(450)
<223> n = A,T,C or G

```

```

<400> 565
ctgcttacgg aagcgctggn tgactaggat gtgatttatt aacgaccaac ttctgttatt 60
tgtgtttaag tttttcatct gtgcatcaaa tcacaaaaag aataaataga gctttttcct 120
ttatcagctc cttgggcaca gcaggctcctg aacacctgcg tctacaatgt tgcataaaga 180
gttcaaaaca caaaataaaa aatattaaga ggaaatcccc atcctgtgac ttgagtcctt 240
taagtctaca ggggctgggt acctcttttt gctaatagga aaatcacatt actacaaat 300
ggggagaaaa ctgtttgcct gtggttagaca cctgcacgca taggattgaa gacagtacag 360
gctgctgtac agagaagcgc ctctcacatc tgaactgcat actgagcggg caagtgcggt 420
gtaagttcag taaaaccctc tgatgatgcc 450

```

```

<210> 566
<211> 563
<212> DNA
<213> Homo sapiens

```

```

<400> 566
acttgagctg tgaggtcatc ggaatccoga cacctgtcct catctggaac aaggtaaaaa 60
ggggtcacta tggagttcaa aggacagaac tctctgcctg tgaccgggac aacctggcca 120
ttcagaccgg ggggtggcca gaaaagcatg aagtaactgg ctgggtgctg gtatctctcc 180
taagtaagga agatgctgga gaatatgagt gccatgcac caattcccaa ggacagggtt 240
cagcatcagc aaaaattaca gtgggttgatg ccttacctga aataccagtg aaaaaagggtg 300
aagggtccga gctataaac tccagaatat tattagtctg catgggttaa agtagtcatg 360
gataactaca ttacctgttc ttgcctaata agtttctttt aatccaatcc actaacatt 420
tagttatatt cactgggttt acacagagaa atacaaaata aagatcacac atcaagacta 480
ctcacaaaaa ttatttatat atttacagaa gaaaagcatg catatcatta aacaataaaa 540
atacttttta tcacaaaaaa aaa 563

```

```

<210> 567
<211> 424
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(424)
<223> n = A,T,C or G

```

```

<400> 567
ccagtgcagca aattgaaaac caactgaaag caaatccaaa tgaggaagat ttaataaag 60
gaataccctt cctccatagca ggtgcaatgc tgactgtctca aggcgtgcgt gcgcgcgcac 120
acacacacac acacacacac atacatactc tcacacacnc atctttccaa ttaaaactgca 180
ggtagaatga gattttgtgt tattcaaaaa atttgtaagt gatcaaaanc actgctatgg 240
aatgcctgtt tatctgcctt tgmtctggtt aaaatctcat aaaaatacat tcaacaggaa 300
aacatanatt gtatgtgtat aaatatatat gtatatatat atattatata cacatgcaca 360
caaatacttt tgttttttga agcataagat agttacataa atactcctat aattgctaaa 420
gttt

```

```

<210> 568
<211> 392
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 568
actggctcac tcagagagga cgtccttcaa ctatgccatg aaggaggctg ctgcagcggc 60
tttgaagaag aaaggatggg aggtgggtgga gtccgacctc tatgccatga acttcaatcc 120
catcatttcc agaaaggaca tcacaggtaa actgaaggac cctgcgaact ttcatgatcc 180
tgccgagctc gttctggcct ataaagaagg ccatctgagc ccagatatgt tgggttganc 240
aaaagaagag ttggaagccn caagaacctt gtgatattcc agttccccct gcantgggtt 300
tgggaagctc ctgccntttt gaaagctggt ttgaagcgaa tgttcatagg aaagtttgct 360
taccacttac cctgcccatg gtangacaaa ag

```

```

<210> 569
<211> 559
<212> DNA
<213> Homo sapiens

```

```

<400> 569
aaagagattt attaaatcat cttatcacaa agatggaaac atatacaaac tagaaacatg 60
caaccatcat cttccacagt caagtccaaa tgtcaaatat ttttcttgc tctgcagatg 120
aaaagttcag atcttatacc caactactta ctacccccga atatttaagt cagtcttctt 180
gaaagtactc agggtagcaa gtaacaaaat gcaaacgatt atataaagaa agtgcagtta 240
aaaaggaaac tatgtggcaa gtaccctctt tcccttccca ccccccaatt aaaggcaaac 300
aatggcactt tgctcttgct taacctagat tgtcttcaaa aactattaaa atgtaaaaga 360
cttaacaaaa aaacaaaaag acgtttaaca gatgtcaaaa agctccttag tgtttgaaaa 420
taaatgtcta aacaaaagac aacatatttt atatacaaca agtttgaaga gccctgaatt 480
gcagcattct gtaacataaa caaacaaaaa gctggtatag gattttattg caaaggcaga 540
atttcttcaa gcagggttaa

```

```

<210> 570
<211> 368
<212> DNA
<213> Homo sapiens

```

```

<400> 570
agccgcgcgt ggaatgctaag tccgatgtca ccaaccagct tgtagatttt cagtggaaac 60
tgggtatggc tgtgagctca gacacttgca gatctcttaa gtatccttac gttgcagtga 120
tgctaaaagt ggcagatcat tcaggccaag taaagaccaa gtgctttgaa atgacgattc 180
cacagtttca gaattttcac agacagttca aggaaattgc tgcagttatt gaaacggtgt 240
gaagacggat tctttggttg ataaattgct atcattctaa agtcatggac ttcactttcg 300

```



gcaacaaaac taaataagga tggaacattt attgaatgaa aaatgcactt ttgtttttcc 360  
attttttt 368

<210> 571  
<211> 261  
<212> DNA  
<213> Homo sapiens

<400> 571  
acacgattgc tgcttcgct atatttgta tataggaatt aagaggatac acacgtttgt 60  
ttcttcgtgc ctgttttatg tgcacacatt aggcattgag acttcaagct ttcttttttt 120  
tgtccacgta tctttgggtc tttgataaag aaaagaatcc ctgttcattg taagcacttt 180  
tacggggctg gtggggaggg gtgctctgct ggtcttcaat taccaagaat tctccaaaac 240  
aattttctgc aggatgattg t 261

<210> 572  
<211> 488  
<212> DNA  
<213> Homo sapiens

<400> 572  
ctctcagctc tcggcgccag gccagcttc ctccaaaatg tctactgttc acgaaatcct 60  
gtgcagctc agcttggagg gtgatcactc tacaccccca agtgcataat ggtctgtcaa 120  
agcctatact aactttgatg ctgagcggga tgctttgaac attgaaacag ccatacaagac 180  
caaaagggtg gatgaggtca ccattgtcaa cattttgacc aaccgcagca atgcacagag 240  
acaggatatt gccttcgctt accagagaag gaccaaaag gaacttgcac cagcactgaa 300  
gtcagcctta tctggccacc tggagacggt gattttgggc ctattgaga cactgtctca 360  
gtatgacgct tctgagctaa aagcttccat gaaggggctg ggaaccgacg aggactctct 420  
cattgagact atctgctcca gaaccaacca ggagctgcag gaaattaaca gagtctacaa 480  
ggaatgt 488

<210> 573  
<211> 619  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(619)  
<223> n = A,T,C or G

<400> 573  
actttactga aagaacacta ntgttctttc ctttcggtt tgaaaaaagt tgtttctgag 60  
gaattgaaac ccagagaagat aactacaaca aaaacatggt aatttttttt taaaaatgat 120  
gattcaaagg cagattttgaa ggaagtaaat atttaggtgg cagaagaagg caaatgcagc 180  
ctctgaaggg aactgttcta attattacct aaaaaataaa gttacacaac tatattcaag 240  
gacatgagat aaagcaactgc ttgaaaacca gaatgactga acagttaggt gaaaaggaaac 300  
agctgaaata ggaaggggaa atggactgaa gaataatttg aatcgggaca gtgatccatc 360  
agtccatagat gcttctggta tgtaaatatc ttgaatcaca ttgtttcctt tcttctgaaa 420  
tctcaaaagg gaattctcac agcactacat taaggttgcc attttgttag gattcaaaat 480  
ttcaatccag tagccatcag gatcttgaat aaatgccagg cctttcattt taccatcatc 540  
aggtttcttc acaaatttga ctccagttt caaccttttc aagcctgac atcaggaaac 600  
caattccata tgaccgatc 619

<210> 574  
<211> 202  
<212> DNA  
<213> Homo sapiens

```

<400> 574
acatccacccc cactatctct tcacataccg aatcaggatt gaaatgtcaa aagatgcact 60
tctctgagaag gcctgtcagtt tggacagctg ctattggaga ataacaaatg ctaaggggtga 120
cgtggaagaa gtccaaggac ctggagtagt tggatgaatt ccaatcatca gccagggtcg 180
ggtatatgaa tacacaagct gt                                     202

```

```

<210> 575
<211> 311
<212> DNA
<213> Homo sapiens

```

```

<400> 575
ccacagttgt atcatatagc atctctaaca ttctatctag gattatctag tatagatctt 60
actatatattg ggactatggt gtatacaatg ttaacaagaa catatcttct ctgcatatat 120
gtgtgaatta taaagaaaag catgagaatg actctaagtt caacaaacat gggatgaatt 180
ctatgtgtct ccagtgctct ggtggggtct ccagcaagc catctctctt tctgtgtctg 240
atattactat tcttttttac attgtgctaa ggaggacaaa agatgagaga tgaataataaa 300
gctttgcctt t                                     311

```

```

<210> 576
<211> 134
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(134)
<223> n = A,T,C or G

```

```

<400> 576
ttttttgcat caaaaagctt tatttccatt tggccaagg cttgttagga tagttaaaaa 60
agctgcctat tggctggagg ganaggctta ggcaaaaacc ctattacttt gcaagggggc 120
cttcaaaagt cgct                                     134

```

```

<210> 577
<211> 488
<212> DNA
<213> Homo sapiens

```

```

<400> 577
ctgatcagtg ggctccaag gaggggctgt aaaaaggagg ccattgtgtg agcctatcag 60
agtgtctgca aacctgaccc ctgctcagta aagcacttgc aaccgtctgt tatgctgtga 120
cacatggccc ctcccctgc caggagcttt ggacctaatt caagcatccc ttggccaga 180
aagaagatgg gggaggaggg agtaataaaa agattgaagt attttgctgg aataagttca 240
aatctctctg aactcaaaact gaggaatttc acctgtaaac ctgagtcgta cagaaagctg 300
cctgtatata caaaaagctt ttatttcctc ctgctcatat tgtgatctcg cctttgggga 360
ctttctttaa accttcagtt atgatttttt ttccatacac ttattggaac tctgcttgat 420
ttttgcctct tccagtcctc ctgacacttt aattaccaac ctgttaccta ctttgacttt 480
ttgcattt

```

```

<210> 578
<211> 476
<212> DNA
<213> Homo sapiens

```

```

<400> 578
accatgcatt aagagcttcc tgattgagat tcagtgcatc agccgtgtct attccatcta 60

```

```

cgctccacc  gtctgtgacc  cactctttga  agctgttgagg  aaaatattca  gcaatgtccg  120
catcaacttg  cagaagaagaa  tataaatgac  atttcaagga  tagaagtata  cctgattttt  180
ttccttttaa  ttttcttggt  gccaatttca  agttccaagt  tgctaataca  gcaacaattt  240
atgaattgaa  ttatcttggt  tgaaaaataa  aagatcactt  tctcagtttt  cataagtatt  300
atgtctcttc  tgagctatatt  catctatatt  tggcagtcgt  aatttttaaa  acccatttaa  360
atttttttcc  ttaccttttt  atttgcattg  ggatcaacca  tcgctttatt  ggctgagata  420
tgaacatatt  gttgaagggt  aatttgagag  aaatatgaag  aactgaggaa  aaaaaa      476

```

```

<210> 579
<211> 246
<212> DNA
<213> Homo sapiens

```

```

<400> 579
ctgggtgtc  ctgagatggt  aggttttctt  attttctctg  tacatctgca  caagctacat  60
ctagaatgaa  gccaccaatt  tcaatgtgac  caggcaatgg  cagccagcac  tgccttacac  120
tggtttgatt  ctgatttcct  aattctggcc  actgcagggt  atgagtaagg  gtggggatca  180
gggagggaag  ccagaagcca  gtctttgtct  ccttttctgt  cttatattta  agtgcctatt  240
tacctg      246

```

```

<210> 580
<211> 615
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1) ... (615)
<223> n = A,T,C or G

```

```

<400> 580
gtcttcacag  taataactaa  tgggtgatcc  taagggtgaaa  ttatttctctt  caaaatagnc  60
atgaactgna  ttccagagag  ggnccagctc  cctacttttg  canatgggaa  agggaggtgc  120
ccaggtgtgg  tctctagac  actggctccg  attgctgccc  ttgaggaagt  agtggtcatt  180
gcacataaac  gtgattttgt  cacttacatt  cacaggccct  gaagaactga  actctccatt  240
caccagcaca  ggatcaggac  agtgcccaa  gcggcactca  gtatgtgtgt  tatccactc  300
cttagaggca  ttgcaaaaaa  ggtcttctt  tctaccagg  tggtagccct  tgatacaaac  360
gtaagtcccc  agaactctgc  cttccacctc  ctttgcgaca  aatatgtcat  tgtccactgg  420
aggaagctct  ggacagtgtc  catctgaagc  agaaactcgc  cagcgaacca  taagacagca  480
cgcacaccaa  aaaaacattc  ggtgatcaaa  gtccctcccc  caggctggaa  tccaccagc  540
tcagacacct  taactgtctc  tgtccctcca  gagttagggc  ttccancaa  ggaactgggc  600
ttaactgact  tccaa      615

```

```

<210> 581
<211> 576
<212> DNA
<213> Homo sapiens

```

```

<400> 581
actcttggtg  agttctgtag  agccttctga  tgtctctaaa  gcactaccga  ttctttggag  60
ttgtcacatc  agataagaca  tatctctaat  tccatccata  aatccagttc  tactattggt  120
gagttctggt  caaagaaaga  aagtttagaa  gctgagacac  aaagggttgg  gagctgatga  180
aactcacaaa  tgatgctgag  aagaagctct  cgacaatacc  cgttggcaag  gagtctcgct  240
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tgtccagaga  aaagagtcct  tgttccagcc  ctattctgcc  actcctgaca  gggtagacct  360
gggtatttgc  aatatttctt  tgggcctctg  ctctctcac  ctaaaaaaag  agaattagat  420
tatattgggt  gtctctcagca  agagaaggag  tatgtgtcca  atgctgcctt  cccatgaatc  480
tgtctccagg  ttatgaatca  gtgggcagga  taaactgaaa  actcccatth  acgtgtctga  540

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atcgagtggag acaaaatttt agtccaata acaagt

576

&lt;210&gt; 582

&lt;211&gt; 939

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 582

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atgagcatcg gctcctctgtg ctgtgcagcc ttgtctctcc tgtgggcagg tccagtgaat 60
gctggtgtgca ctcagaccccc aaaattccag gtctgaaga caggacagag catgacactg 120
cagtggtgccc aggatatgaa ccatgaatac atgtcctggt atcgacaaga cccaggcatg 180
gggctgagggc tgattcatta ctcagttggt gctgggatca ctgaccaagg agaagtcacc 240
aatggctaca atgtctccag atcaaccaca gaggatttcc cgctcagggt cgtgtcgggt 300
gctccctccc agacatctgt gtacttctgt gccagcagtt actcagtcgg ggagggcggg 360
gattcacccc tccactttgg gaatgggacc aggtctactg tgacagagga cctgaacaag 420
gtgttcccac ccgaggtcgc tgtgtttgag ccatcagaag cagagatctc ccacacccaa 480
aaggccacac tgggtgtgct ggccacaggg ttcttccctg acccagtgga gctgagctgg 540
tgggtgaatg ggaaggaggt gcacagtggt gtccagcagg acccgagcc cctcaaggag 600
cagcccgccc tcaatgactc cagatctgct ctgagcagcc gccctgaggt ctcggccacc 660
ttctggcaga acccccgcaa ccacttccgc tgtcaagtcc agttctacgg cctctcggag 720
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tggggtagag cagactgtgg ctttacctcg gtgtcctacc agcaagggtt cgtgtctgac 840
accatcctct atgagatcct gctagggaa gcccacctgt atgctgtgct ggtcagcgcc 900
cttgtgttga tggccatggt caagagaaa gatttctga 939

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&lt;210&gt; 583

&lt;211&gt; 828

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 583

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atgaactatt ctccaggctt agtatctctg atactcttac tggctggaag aaccogtga 60
aattcagtga ccagatgga agggccagtg actctctcag aagaggcctt cctgactata 120
aactgcacgt acacagccac aggataccct tcccttttct ggtatgtcca atatcctgga 180
gaaggtctac agtctcctct gaaagccacg aaggctgatg acaagggaag caacaaaggt 240
tttgaagcca cataccgtaa agaaccact tctttccact tggagaaaag ctcagttcaa 300
gtgtcagact cagcgggtga ctctgtgct cogaacctct ctctcaggg cggatctgaa 360
aagctggtct ttggaagggg aacgaaactg acagtaaaac catatatcca gaacctctgac 420
cctgcctggt accagctgag agactctaaa tccagtgaca agtctgtctg cctattcacc 480
gattttgatt ctcaaacaaa tgtgtcacia agtaaggatt ctgatgtgta tatcacagac 540
aaaaactgtg tagacatgag gtctatggac ttcaagagca acagtgtctg ggctgtggag 600
aacaactctg actttgcatg tgcaaacgcc ttcaacaaca gcattattcc agaagacacc 660
ttcttcccca gcccgaaaag ttctgtgat gtcaagctgg tccgagaaaag ctttgaacaa 720
gatacgaacc taacctttca aaacctgtca gtgattgggt tccgaactct cctcctgaaa 780
gtggccgggt ttaactctgct catgaectg cggtgtgggt ccagctga 828

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&lt;210&gt; 584

&lt;211&gt; 275

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 584

```

Met Asn Tyr Ser Pro Gly Leu Val Ser Leu Ile Leu Leu Leu Gly
      5              10              15
Arg Thr Arg Gly Asn Ser Val Thr Gln Met Glu Gly Pro Val Thr Leu

```

20 25 30  
 Ser Glu Glu Ala Phe Leu Thr Ile Asn Cys Thr Tyr Thr Ala Thr Gly  
 35 40 45  
 Tyr Pro Ser Leu Phe Trp Tyr Val Gln Tyr Pro Gly Glu Gly Leu Gln  
 50 55 60  
 Leu Leu Leu Lys Ala Thr Lys Ala Asp Asp Lys Gly Ser Asn Lys Gly  
 65 70 75 80  
 Phe Glu Ala Thr Tyr Arg Lys Glu Thr Thr Ser Phe His Leu Glu Lys  
 85 90 95  
 Gly Ser Val Gln Val Ser Asp Ser Ala Val Tyr Phe Cys Ala Pro Asn  
 100 105 110  
 Pro Ser Leu Gln Gly Gly Ser Glu Lys Leu Val Phe Gly Lys Gly Thr  
 115 120 125  
 Lys Leu Thr Val Asn Pro Tyr Ile Gln Asn Pro Asp Pro Ala Val Tyr  
 130 135 140  
 Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr  
 145 150 155 160  
 Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val  
 165 170 175  
 Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp Phe Lys  
 180 185 190  
 Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala  
 195 200 205  
 Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser  
 210 215 220  
 Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr  
 225 230 235 240  
 Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile  
 245 250 255  
 Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu  
 260 265 270  
 Trp Ser Ser  
 275

&lt;210&gt; 585

&lt;211&gt; 312

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 585

Met Ser Ile Gly Leu Leu Cys Cys Ala Ala Leu Ser Leu Leu Trp Ala  
 5 10 15  
 Gly Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu  
 20 25 30  
 Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His  
 35 40 45  
 Glu Tyr Met Ser Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu  
 50 55 60  
 Ile His Tyr Ser Val Gly Ala Gly Ile Thr Asp Gln Gly Glu Val Pro  
 65 70 75 80  
 Asn Gly Tyr Asn Val Ser Arg Ser Thr Thr Glu Asp Phe Pro Leu Arg  
 85 90 95  
 Leu Leu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser  
 100 105 110  
 Ser Tyr Ser Val Gly Glu Gly Asp Ser Pro Leu His Phe Gly Asn  
 115 120 125  
 Gly Thr Arg Leu Thr Val Thr Glu Asp Leu Asn Lys Val Phe Pro Pro

130 135 140  
 Glu Val Ala Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln  
 145 150 155 160  
 Lys Ala Thr Leu Val Cys Leu Ala Thr Gly Phe Phe Pro Asp His Val  
 165 170 175  
 Glu Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser  
 180 185 190  
 Thr Asp Pro Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg  
 195 200 205  
 Tyr Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn  
 210 215 220  
 Pro Arg Asn His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu  
 225 230 235 240  
 Asn Asp Glu Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val  
 245 250 255  
 Ser Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Val Ser  
 260 265 270  
 Tyr Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu  
 275 280 285  
 Gly Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met  
 290 295 300  
 Ala Met Val Lys Arg Lys Asp Phe  
 305 310

&lt;210&gt; 586

&lt;211&gt; 97

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 586

Glu Val Glu Val Ser Arg Asp His Ala Ser Leu Gly Asp Ser Glu Thr  
 5 10 15  
 Leu Ser Gln Thr Glu Leu Arg Lys Lys Glu Arg Lys Lys Lys Arg Glu  
 20 25 30  
 Arg Lys Phe Gln Ala Asn Cys Gly Ile Asp Phe Ile Ile Phe Trp Ile  
 35 40 45  
 Phe Trp Ile Leu Leu Phe Ser His His Trp Ile Gln Glu Ser Leu Leu  
 50 55 60  
 Cys Pro Pro Ser Pro Lys Glu Val Thr Cys Arg Glu Met Leu Thr Gly  
 65 70 75 80  
 Gly Cys Leu Pro Trp Ala Thr Arg Ser His Leu Gly Arg Arg Lys Cys  
 85 90 95  
 Ser

&lt;210&gt; 587

&lt;211&gt; 16

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 587

Phe Gln Ala Asn Cys Gly Ile Asp Phe Ile Ile Phe Trp Ile Phe Trp  
 1 5 10 15